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RATE OF REGENERATION OF SENSORY NERVE FIBERS

SYDNEY SUNDERLAND, M.D., D.Sc.
MELBOURNE, AUSTRALIA

THIS paper is concerned with the rate of regeneration of sensory fibers, calculated on the basis of the rate of advance of Tinel's sign, during the recovery of injured peripheral nerves. Though it is generally accepted that the eliciting of Tinel's sign is evidence of the presence of "young axis-cylinders in the process of regeneration," there has been no histologic confirmation of the structure of the fiber at the site of percussion. The present account is not concerned either with the morphologic features of the recovering nerve fiber or with the prognostic significance of the sign, but is confined to a consideration of the rate at which it advances.

With the exception of Seddon, Medawar and Smith,[1] those who have devoted attention to the estimation of rates of recovery on this basis have omitted to indicate whether, in any instance, this was obtained by a single calculation or from data provided by successive examinations spread over the process of recovery; furthermore, they give the impression that in any individual case the rate is constant throughout the process of repair. An advancing Tinel's sign, however, presents an opportunity of studying the rate of growth of sensory fibers, in any individual case, over different segments of the nerve and at various periods after injury and suture; thus, it should be possible to ascertain whether the rate is constant or whether it diminishes progressively. For calculation of the rate by successive examinations, it is not necessary to know the duration of the initial delay, i. e., the delay occurring at the site of the lesion before the axons begin to grow down the distal segment. This is an advantage, since there is no method of accurately estimating this period in any individual case except when Tinel's sign can be recognized immediately below the lesion.

The observations of Seddon, Medawar and Smith[1] were made on 6 sutured nerves provided by 4 patients. They appear to have

From the Department of Anatomy and Histology, University of Melbourne.

1. Seddon, H. J.; Medawar, P. B., and Smith, H.: Rate of Regeneration of Peripheral Nerves in Man, J. Physiol. **102**:191-215 (Sept. 30) 1943.

been convinced, however, that the rate was constant and, on the graph obtained by plotting time against distance, constructed a straight growth line representing a constant rate in spite of two indications to the contrary:

1. The latent period, obtained by extrapolation, had a negative value in 5 of the cases.

2. A curve would have suited their findings in some cases just as satisfactorily, particularly if certain discrepant readings had been discarded. For example, in their figure 8, retrogression, rather than advance, of Tinel's sign is shown by the fourth and fifth readings for the ulnar nerve and by the fifth and sixth readings for the median nerve. In these cases an analysis of the data strongly suggests a progressively diminishing rate.

MATERIAL

Eleven patients provided 12 peripheral nerve injuries on which the observations here reported were based. In 3 cases the lesion was of the type defined as axonotmesis; in the remaining 9 cases the nerve had been sutured. The distances and times in each case were accurately measured. The sign was elicited by gentle and localized percussion, and, so far as was possible, precautions were taken to avoid transmission of the force to segments of the nerve proximal to the site of percussion. The number of observations on each nerve was not constant, since the sign was not elicited at every examination; thus it was not possible in every case to determine whether the rate was a constant or a diminishing one.

It is not claimed that final conclusions can be drawn from such a small series of cases. It is hoped that other workers in this field will make similar contributions, so that a series of cases sufficiently large and detailed for statistical analysis can be gathered from a number of sources. It is regrettable that this sign has been studied in detail by few who have investigated the regeneration of nerves. In almost every instance there has been no more than a brief reference to Tinel's sign, when so much could have been learned from precise measurements of time and distance made at successive examinations throughout the period of recovery.

OBSERVATIONS

Full details relating to the progress of Tinel's sign and the calculated rate of regeneration in each nerve are given in the table, and only brief case reports are given here.

Case 24.—W. J. A. sustained a gunshot wound of the left ulnar nerve in the medial epicondylar groove on July 1, 1941. There was complete interruption of conduction in the nerve, which, however, was intact when seen in the wound. The nerve recovered spontaneously.

Case 94.—M. G. sustained a perforating gunshot wound of the right thigh on Oct. 26, 1942, which resulted in complete interruption of conduction in the sciatic nerve. Spontaneous recovery occurred in the medial popliteal division but

Details Relating to Advance of Tinel's Sign and Rate of Regeneration Calculated Therefrom

Nerve; Nature of Nerve Injury	Case No.	Date of Injury	Date of Suture	Date of Examination *	Time, Days	Level of Tinel's Sign Below Lesion, Mm.	Distance Traveled by Axons, Mm.	Rate of Regeneration, Mm. per Day
Median								
Suture	322	10/21/44	2/21/45	9/27/45 (218)		180		
					54		90	1.7
				11/20/45 (272)		270		
					114		85	0.7
				3/14/46 (386)		355		
					19		15	0.8
				4/ 2/46 (405)		370		
					100		60	0.6
				7/11/46 (505)		430		
Ulnar								
Lesion in continuity	24	7/ 1/41	.....	8/ 9/41 (39)		100		
					111		170	1.5
				11/28/41 (150)		270		
Suture	105	12/22/42	12/24/42	3/ 5/43 (71)		150		
					41		100	2.4
				4/15/43 (112)		250		
	127	12/ 8/42	2/ 2/43	5/18/43 (105)		190		
					63		80	1.3
				7/20/43 (168)		270		
	182	5/17/41	9/24/43	11/ 9/43 (46)		130		
					63		120	1.9
				1/11/44 (109)		250		
	290	4/ 3/44	4/ 4/44	5/ 7/44 (33)		15		
					38		95	2.5
				6/14/44 (71)		110		
					92		180	2.0
				9/14/44 (163)		290		
					36		30	0.8
				10/20/44 (199)		320		
	322	10/21/44	6/ 6/45	9/27/45 (113)		200		
					54		85	1.6
				11/20/45 (167)		285		
					114		70	0.6
				3/14/46 (281)		355		
					19		15	0.8
				4/ 2/46 (300)		370		
					100		50	0.5
				7/11/46 (400)		420		
Sciatic								
Lesion in continuity	270	6/30/43	.....	3/15/44 (258)		100†		
					124		200	1.6
				7/17/44 (382)		300†		
					116		40	0.3
				11/10/44 (498)		340†		
Suture	94	10/26/42	2/ 5/45	5/24/45 (108)		280		
					98		160	1.6
				8/30/45 (206)		440		
					42		50	1.2
				10/11/45 (248)		490		
					42		30	0.7
				11/22/45 (290)		520		
					222		110	0.5
				7/ 2/46 (512)		630		
	122	12/28/42	9/ 4/43	1/11/44 (129)		280		
					121		260	2.1
				5/11/44 (250)		540		
					70		100	1.4
				7/20/44 (320)		640		
	137	10/31/42	7/19/44	12/ 6/44 (140)		300		
					166		270	1.6
				5/21/45 (306)		570		
Lateral popliteal								
Lesion in continuity	174	4/ 7/43	.....	3/ 9/44 (337)		150		
					98		70	0.7
				6/15/44 (435)		220		

* The figure in parentheses after each date is the number of days between the time of suture (or injury in cases of axonotmesis) and the time of the examination.

† Measurements taken from the head of the fibula.

was so little advanced in the lateral popliteal division that the nerve was explored on Feb. 5, 1945. The partially severed lateral division was repaired. The progress of Tinel's sign, measured from the level of the suture, and the rates calculated refer to the lateral popliteal division of the nerve.

CASE 105.—K. T. F. lacerated his right elbow on a piece of glass on Dec. 22, 1942. The ulnar nerve had been divided at a point 5 cm. below the medial epicondyle of the humerus and was sutured two days later.

CASE 122.—P. H., on Dec. 28, 1942, sustained a perforating gunshot wound of the left buttock, with a comminuted fracture of the acetabulum and the head and neck of the femur. The sciatic nerve, which was completely severed, was not sutured until Sept. 4, 1943.

CASE 127.—D. F. W. sustained a laceration of the right elbow on Dec. 8, 1942, which resulted in complete interruption of conduction in the ulnar nerve. At exploration, on Feb. 2, 1943, the nerve was observed to be severed in the medial epicondylar groove. It was sutured.

CASE 137.—C. G. W. sustained a penetrating gunshot wound of the left thigh on Oct. 31, 1942, which resulted in a fracture of the middle third of the femur and severance of the sciatic nerve. The nerve was sutured on July 19, 1944.

CASE 174.—S. E. N. sustained a gunshot wound of the right knee in the region of the neck of the fibula on June 12, 1941. At an operation on the infected upper end of the fibula, on April 7, 1943, the lateral popliteal nerve was damaged and conduction completely interrupted. The nerve recovered spontaneously, but restoration of function was not complete.

CASE 182.—J. S., on May 17, 1941, sustained a gunshot wound of the right elbow with a fracture of the lower end of the humerus and complete interruption of conduction in the ulnar and median nerves. The patient was a prisoner of war, and I did not examine him until July 13, 1943, when the median nerve was recovering but interruption of conduction in the ulnar nerve was still complete. On Sept. 24, 1943 the ulnar nerve was explored, sutured just above the medial epicondyle of the humerus and transposed anterior to it. This case is of interest in view of the long period intervening between the injury and the suture of the nerve.

CASE 270.—J. L. W. sustained a perforating gunshot wound of the left buttock on June 30, 1943, which fractured the femur. There was complete interruption of conduction in the sciatic nerve, which was intact when seen in the wound. Spontaneous recovery in the medial popliteal division was satisfactory; the only recovery recorded for the lateral division was an advancing Tinel sign.

CASE 290.—A. B. R. was involved in an automobile accident on April 3, 1944, in which he sustained a laceration of the right elbow. The ulnar nerve was severed in the medial epicondylar groove of the humerus and was sutured the day after the injury.

CASE 322.—O. A. R. sustained a gunshot wound of the upper third of the left arm on Oct. 21, 1944, which completely severed the ulnar and median nerves and the brachial artery.

On Feb. 21, 1945, the median nerve was sutured under moderate tension and the ulnar nerve under such considerable tension that it was thought advisable to reexplore and resuture it on June 6, 1945, at which time the union was effected without tension.

This is an interesting case in that the nerves were damaged at about the same level. After suture, Tinel's sign had advanced 200 mm. in one hundred and thirteen days in the ulnar nerve and 180 mm. in two hundred and eighteen days in the median nerve. The difference in the distances covered is not necessarily due to a faster rate of growth of the ulnar axons; it could be attributed to the more accurate operative apposition of the stumps of the ulnar nerve, resulting in a shorter delay at the site of suture before the entry of axons into the distal segment. That the latter is the more likely explanation is supported by the observation that farther distally the calculated rates for the two nerves approximated each other.

CONCLUSIONS

In analyzing the results, it should be borne in mind that the value obtained for the rate of regeneration will depend on the length of the nerve over which it is measured. Over considerable lengths a gradual slowing of the regenerative processes would result in a reduced over-all calculation for the rate, while over very short lengths the calculated rate would be greater in the early stages. Frequent readings over short distances will give the most accurate results.

The reported observations demonstrate that after suture regenerating sensory fibers advance at a progressively diminishing rate. The following generalizations appear to be justified cases of suture in the proximal part of the limb.

1. In the early stages of recovery (up to one hundred and twenty days) the rate fell from 2.5 to 2 mm. per day. The distances over which the calculations were made varied from 95 to 120 mm.—it is probable that the early rate would have approximated 3 mm. per day had the calculations been based on more frequent readings at this stage.

2. In the intermediate stages of recovery (from one hundred and twenty to two hundred days) the rate was approximately 1.6 mm. per day.

3. Over the terminal stages of recovery (two hundred to five hundred days) the rate fell from 0.8 to 0.5 mm. per day. In this phase the rate was, in most instances, calculated over very short distances (15, 15, 30, 30, 40, 50, 60, 70, 70, 85 and 110 mm.).

The results are comparable with those previously obtained for regenerating motor fibers,[2] for which, it was believed, the method employed gave the rate of advance of functionally mature fibers. The question of functional maturity requires further definition, but the opinion was expressed by Gutmann, Guttmann, Medawar and Young[3] and by

2. Sunderland, S.: Course and Rate of Regeneration of Motor Fibers Following Lesions of the Radial Nerve, Arch. Neurol. & Psychiat. **56**:133-157 (Aug.) 1946; Rate of Regeneration of Motor Fibers in the Ulnar and Sciatic Nerves, ibid., this issue, page 7.

3. Gutmann, E.; Guttmann, L.; Medawar, P. B., and Young, J. Z.: The Rate of Regeneration of Nerve, J. Exper. Biol. **19**:14-44 (May) 1942.

Seddon, Medawar and Smith [1] that the process implied in the use of the term advances at a slower rate than does growth of the axon tips, which is revealed by the advance of Tinel's sign. The present findings, however, suggest that, though the processes in the two types of fibers (motor and sensory) may not be identical in nature, there is no significant difference in their rates of advance as calculated by the two methods. The figures given by Seddon and associates [1] also support this suggestion (1.6 ± 0.2 mm. per day for functionally mature motor fibers following suture and an average rate of 1.71 mm. per day for the progress of Tinel's sign following suture), though the authors themselves stated that "the wave front for Tinel's sign" should be "well in front of that for motor and sensory fibers that have advanced to functional maturity."

In a later, final, report [4] on the rate of regeneration in human peripheral nerves, attention will be directed to the nature of the process which is being measured when the rate of regeneration is calculated, and to the significance of the various criteria on which the different methods depend.

SUMMARY

Observations on the rate of advance of Tinel's sign demonstrate that after suture in the proximal part of the limb regenerating sensory fibers advance at a progressively diminishing rate, which in the initial stages may be as great as 3 mm. per day. It gradually slows until it reaches a value of approximately 0.5 mm. per day over the terminal stages of recovery.

The National Health and Medical Research Council of Australia made a grant in aid of this investigation.

University of Melbourne.

4. Sunderland, S.: Rate of Regeneration in Human Peripheral Nerves and Analysis of Interval Between Injury and Onset of Recovery, Arch. Neurol. & Psychiat., to be published.

RATE OF REGENERATION OF MOTOR FIBERS IN THE ULNAR AND SCIATIC NERVES

SYDNEY SUNDERLAND, M.D., D.Sc.
MELBOURNE, AUSTRALIA

IN A PREVIOUS paper [1] a method for estimating the rate of growth of functionally mature motor fibers in human peripheral nerves was reported, together with clinical observations on the course and rate of regeneration after lesions of the radial nerve. In the present paper, which deals with the rate of advance of motor fibers after lesions of the ulnar and sciatic nerves, the investigation was conducted as for the radial nerve, and reference should be made to the original paper for a detailed account of the method employed to calculate the rate and the criteria adopted in selecting the clinical material.

The rate of regeneration, R, in millimeters per day, is expressed by the formula:

$$R = \frac{L^2 - L^1}{T^2 - T^1}$$

L^1 and L^2 are the shortest distances to two muscles from a point on the nerve proximal to the site of origin of its branches. Values for these lengths were obtained for a series of muscles from an anatomic investigation of the ulnar and sciatic nerves.[2] The lengths were measured directly along the nerve and its branches between a selected point on the nerve and the site of entry of the branch into the muscle. If more than one branch supplied a muscle, the measurement selected was the shortest route available. The position of the point, however, is immaterial, since the distance along the nerve to the more proximally innervated muscle is common to the measurement for each muscle. For reasons detailed in the original paper, this formula should not be employed when a considerable distance separates the muscles. By the

From the Department of Anatomy and Histology, University of Melbourne.

1. Sunderland, S.: The Course and Rate of Regeneration of Motor Fibres Following Lesions of the Radial Nerve, Arch. Neurol. & Psychiat. **56**:133-157 (Aug.) 1946.

2. Sunderland, S., and Hughes, E. S. R.: The Metrical and Non-Metrical Features of the Muscular Branches of the Ulnar Nerve, J. Comp. Neurol. **85**:113-126 (Aug.) 1946; The Metrical and Non-Metrical Features of the Muscular Branches of the Sciatic Nerve and Its Medial and Lateral Popliteal Divisions, ibid. **85**:205-222 (Oct.) 1946.

selection of suitable muscles, the rate should be calculated independently over several short sections of the nerve. This reduces to a minimum inaccuracies due to (*a*) the fact that the rate normally diminishes as the axons advance and (*b*) variations in the delay occurring within a muscle before recovery appears.

T^1 and T^2 signify the times taken to reinnervate the two muscles, calculated in days from the date of injury or nerve suture to the date of the onset of recovery. To qualify for selection, it was necessary for the cases to fulfil the following conditions:

1. Interruption of conduction must be complete and associated with wallerian degeneration.

2. The onset and progress of recovery must be such as to suggest uniform involvement of the fibers at the site of injury.

3. The onset and progress of recovery must be such as to suggest that the axons had commenced to regenerate at about the same time.

4. Any departure from the normal order of recovery should be capable of satisfactory explanation on the basis of established anatomic variations.

5. In order to detect the earliest signs of recovery in individual muscles, the patients are to be examined at intervals not exceeding a week until all muscles are contracting. In 2 cases in which intervals of two to four weeks occurred between examinations, muscles showing recovery at the second examination were considered to have recovered midway between the two examinations. It is an advantage for all observations to be made by the same observer (as in the present inquiry), since this reduces the personal factor introduced by the transferring of patients from clinic to clinic.

Advantages of the method are (1) that it renders unnecessary a knowledge of the level of the injury and the initial delay before the commencement of regeneration and (2) that the rate of regeneration can be estimated separately over different segments of the nerve by selecting muscles which are innervated at different levels. By this means it is possible to ascertain whether or not regeneration proceeds uniformly during the entire process. It is not possible, however, to estimate the rate over the section of the nerve proximal to the origin of its first branch.

L and T are used throughout the text to signify $L^2—L^1$ and $T^2—T^1$.

The rate of regeneration can be estimated in any individual case, or an average rate, calculated from mean readings for T, can be obtained from observations on a large series of cases. In an individual case it is necessary to take into consideration the considerable and unpredictable range of variation in the length of the shortest fibers to any given

muscle. This factor was apparently disregarded by Seddon, Medawar and Smith.[3] When mean readings for L and T are obtained from a number of cases, as in the present inquiry, it is believed that this unpredictable element is reduced to a minimum. By taking average readings for L and T for any group of muscles, factors are disregarded which are peculiar to an individual case and which may influence the rate. Regardless of the method employed, however, the rate in any individual case can be calculated only in retrospect—that is, after regeneration has advanced over suitable lengths of the nerve. For this to be possible the length must be known, and there is no way of obtaining this in the living subject; recourse must therefore be made to the values provided by the cadaver, and these show a wide range of variation.

MATERIAL

The observations are based on a series of 106 lesions of the ulnar nerve and 67 lesions of the sciatic nerve (main trunk and medial and lateral popliteal divisions) occurring in 301 consecutive cases of peripheral nerve injuries which I studied over the period from 1941 to 1946 at an Australian military hospital and at the Repatriation Clinic, Melbourne. The case histories are to be reported in detail elsewhere. Of the series, only 21 lesions of the ulnar and 16 lesions of the sciatic nerve were suitable for the present inquiry.

ULNAR NERVE

The only muscles appropriately spaced to permit a calculation of the rate of regeneration by the use of the formula were the hypothenar group and the first dorsal interosseous muscle. Thus, the rate could be calculated only over the terminal portion of the nerve.

Distance.—The length, L, in each of 20 specimens is given in table 1. In the preliminary anatomic investigations, the distance was measured from the level of the tip of the styloid process of the radius to each of the three hypothenar muscles. Clinically, however, it was not always possible at the onset of recovery to detect which fibers of the group were contracting. For this reason, the hypothenar muscles have been considered as a single anatomic unit, and in arriving at a value for L (i. e., L^2—L^1) the shortest distance to the first hypothenar muscle to be supplied was taken as the distance to the group.

Time.—The onset of recovery in the hypothenar and the first dorsal interosseous muscles following axonotmesis (11 patients) and suture (10 patients), together with values for T, are given in table 2, which also contains details relating to the cause and the level of the injury. The mean and the standard deviation for T are given in table 5.

3. Seddon, H. J.; Medawar, P. B., and Smith, H.: Rate of Regeneration of Peripheral Nerves in Man, J. Physiol. **102**:191-215 (Sept. 30) 1943.

TABLE 1.—*Values for $L^2 - L^1$ (L)**

Specimen	H and D1	G and FDL	G and FHL	PL and EHL	TA and EHL
1	†	106	116	69	43
2	67	131	220	89	67
3	†	151	183	86	71
4	46	153	204	98	64
5	63	158	155	106	72
6	51	162	214	137	135
7	63	141	194	75	72
8	45	125	206	104	77
9	37	72	186	115	83
10	52	133	182	29	35
11	33	165	170	62	84
12	34	‡	‡	42	110
13	58	120	191	130	121
14	63	135	198	99	82
15	56	174	133	45	23
16	54	202	183	27	48
17	23	166	201	130	100
18	45	142	126	84	79
19	44	127	233	103	97
20	54	135	178	117	100
Mean	49	142	182	87	78
Standard deviation	12	28	31	33	28

* The distances (in millimeters) are based on measurements taken from the level of the tip of the styloid process of the radius for the ulnar nerve and from a level 5 cm. above the medial epicondyle of the femur for the sciatic nerve and its divisions. H indicates the hypothenar muscles; D 1, first dosal interosseous muscles; G, gastrocnemius; FDL, flexor digitorum longus; FHL, flexor hallucis longus; TA, tibialis anterior; PL, peroneus longus, and EHL, extensor hallucis longus.

† The first dorsal interosseous muscle was supplied partly or completely by the median nerve.

‡ In this specimen, the first branch of the gastrocnemius left the nerve above the 5 cm. level, so that values could not be obtained for these two sections on the same basis as for the others.

TABLE 2.—*Lesions of the Ulnar Nerve (Axonotmesis and Suture)*

Causative Injury; Nature of Nerve Injury	Case No.	Level of Injury, Mm.*	MHE to RSL, Mm.	Interval, in Days, Between Injury and Suture	Return of Voluntary Contraction, Weeks		
					H	D 1	$T^2 - T^1$
Axonotmesis							
Laceration	103	50 above RSL	...	...	20	32	12
	323	20 below RSL	...	...	8	20	12
Gunshot wound	30	200 above RSL	...	...	62	79	17
	31	100 above MHE	280	...	80	91	11
	129	60 above MHE	260	...	90	107	17
	136	170 above MHE	290	...	29	41	12
	179	80 above MHE	270	...	22	30	8
	237	80 above RSL	...	...	34	42	8
Gunshot wound + bone injury	43	130 above RSL	...	...	53	61	8
	176	140 above RSL	...	...	32	39	7
	235	10 above RSL	...	...	29	40	11
Suture							
Compound fracture of radius and ulna	328	150 above RSL	295	177	32	42	10
Laceration	105	250 above RSL	300	2	40	65	25
	139	10 above RSL	...	Immediate	28	51	23
	158	25 above MHE	275	104	85	109	24
	269	265 above RSL	290	277	46	62	16
	290	At MHE	250	1	81	102	21
	325	80 above RSL	...	5	40	54	14
Gunshot wound	38	80 above RSL	...	191	17	47	30
	207	60 above MHE	260	131	67	81	14
Gunshot wound + bone injury	243	90 above MHE	265	Immediate	37	55	18

* H indicates hypothenar muscles; D 1, first dorsal interosseous muscle; RSL and MHE, levels of the styloid process of the radius and the medial epicondyle of the humerus, respectively.

Results.—The mean rate of regeneration was 0.6 mm. per day after "axonotmesis" and 0.4 mm. per day after suture.

In studying the influence of individual variations in L and T, it is reasonable to assume that high values for T ($T+$) would probably mean that the distance traveled was greater in that patient, while low values for T ($T-$) would probably be associated with shorter distances. Calculations made on this basis (using the standard deviations) for both types of lesions gave the following rates:

	L+ T+	L− T−
Following axonotmesis	0.6 mm. per day	0.7 mm. per day
Following suture.....	0.3 mm. per day	0.4 mm. per day

Comment.—Over the terminal portion of the nerve, functional regeneration proceeded at the rate of about 0.6 mm. per day after axonotmesis and 0.4 mm. per day after suture. The corresponding rates for the terminal portion of the radial nerve (posterior interosseous division) were 0.8 and 0.6 mm. per day. The interval, T, did not vary significantly with the level of the injury; apparently, the rate of growth for the terminal portion of the nerve is not influenced by the level of the injury; that it is related to the duration of the latent period intervening between the injury and the first appearance of recovery (after allowing for the influence of the level of the injury on this period) has been suggested by previous inquiries (Seddon, Medawar and Smith [3]; Sunderland [1]). This matter will be more fully discussed in a subsequent report.

SCIATIC NERVE AND ITS MEDIAL AND LATERAL POPLITEAL DIVISIONS

The rate of regeneration was measured over the sections of the medial and lateral popliteal nerves representing the following levels of innervation: gastrocnemius to flexor digitorum longus; gastrocnemius to flexor hallucis longus; tibialis anterior to extensor hallucis longus, and peroneus longus to extensor hallucis longus. These sections cover what might be regarded as the intermediate portion of the sciatic nerve.

Distance.—The length, L, for each of these sections in 20 specimens is given in table 1.

Time.—The onset of recovery following axonotmesis (15 patients, presenting 16 lesions—in case 245 the lesion was bilateral) in the different muscles concerned and information relating to the cause and the level of the injury are given in table 3. Values for T are given in table 4.

Results.—The mean rates of regeneration, calculated in millimeters per day, over the selected sections of the nerve are given in table 5; the estimated rates for the high and low values (standard deviations) of the lengths and times, respectively, are also included.

TABLE 3.—*Lesions of the Sciatic, Medial Popliteal and Lateral Popliteal Nerves (Axonotmesis)*

Nature of Causative Injury	Case No.	Level of Injury, Mm.	Return of Voluntary Contraction, Weeks *					
			G	FDL	FHL	TA	PL	EHL
Simple compression.....	188	Neck of fibula	..	..	..	21	21	36
	245	Neck of fibula	..	..	..	24	20	36
	245	Neck of fibula	..	..	..	18	18	30
Simple fracture of femur.	326	100 above MFE†	29	46	53	43	44-48	49
Gunshot wound.....	82	Head of fibula	..	..	..	18	18	35
	88	Lower third of thigh	..	..	..	102	111	111
	95	50 above MFE	15	24	29	24	19	33
	109	70 above MFE	13	21	21	13	13	21
	112	230 above MFE	26	33	41	28	28	23
	145	160 above MFE	18	37	42	27	27	36
	190	At MFE	22	42	42	..	..	..
	240	150 above MFE	..	..	..	37	31	44
	254	Head of fibula	..	..	..	7	7	12
Gunshot wound + bone injury.....	150	Midthigh	..	..	..	13	13	21
	260	50 above MFE	12	35	35	..	..	..
	293	Midthigh	..	..	..	71	59	80

* G indicates gastrocnemius; FDL, flexor digitorum longus; FHL, flexor hallucis longus; TA, tibialis anterior; PL, peroneus longus, and EHL, extensor hallucis longus.

† MFE indicates medial epicondyle of the femur.

TABLE 4.—*Values for* $T^2 - T^1$ *(T)*

Nature of Causative Injury	Case No.	Times, in Weeks *			
		G and FDL	G and FHL	TA and EHL	PL and EHL
Simple compression.....	188	..	..	15	15
	245	..	..	12	16
	245	..	..	12	12
Simple fracture of femur.....	326	17	24	6	3
Gunshot wound.....	82	..	..	17	17
	88	..	..	9	..
	95	9	14	9	14
	109	8	8	8	8
	112	7	15	5	5
	145	19	24	9	9
	190	20	20	..	..
	240	..	..	7	13
	254	..	..	5	5
Gunshot wound + bone injury	150	..	..	8	8
	260	23	23	..	..
	293	..	..	9	21
Mean.....		14.7	18.3	9.4	11.2
Standard deviation.....		6.5	6.1	3.5	5.4

* G indicates gastrocnemius; FDL, flexor digitorum longus; FHL, flexor hallucis longus; TA tibialis anterior; PL, peroneus longus, and EHL, extensor hallucis longus.

Comment.—Since the regenerating nerve fiber advances at a diminishing rate, the distance over which the rate is calculated should be sufficiently short to reduce or eliminate the influence of this factor. In the case of the two sections (*a*) gastrocnemius to flexor digitorum longus and (*b*) gastrocnemius to flexor hallucis longus, it is believed that the discrepancy in the rates could be due to the long distances involved in the calculations. Against this, however, is the observation that when the lengths *L*, *L*+ and *L*— for both sections are arranged in numerical order, the corresponding rates do not progressively decrease as the length increases but show certain conflicting irregularities; the fastest rate is, however, associated with the shortest distance. In the case of the two sections of the nerve, (*a*) tibialis anterior to extensor

TABLE 5.—Rates *of Regeneration, in Millimeters per Day*

Nerve Segment over Which Rate Was Estimated *	Distance, L, in Mm.	Time, T, in Weeks	Mean Rate Calculated from Mean L and T	Rate Estimated from L+ and T+ †	Rate from L— and T— †
Ulnar nerve					
H and D 1	49 ± 12				
Axonotmesis	.....	11.2 ± 3.4	0.6	0.6	0.7
Suture	.....	19.5 ± 6.1	0.4	0.3	0.4
Sciatic nerve					
Axonotmesis					
G and FDL	142 ± 28	14.7 ± 6.5	1.4	1.1	2.0
G and FHL	182 ± 31	18.3 ± 6.1	1.4	1.2	1.8
TA and EHL	78 ± 28	9.4 ± 3.5	1.2	1.2	1.2
PL and EHL	87 ± 33	11.2 ± 5.4	1.1	1.0	1.3

* H indicates hypothenar muscles; D 1, first dorsal interosseous muscles; G, gastrocnemius; FDL, flexor digitorum longus; FHL, flexor hallucis longus; TA, tibialis anterior; EHL, extensor hallucis longus, and PL, peroneus longus.

† L+ and T+ indicate high values, and L— and T— low values, for length and time.

hallucis longus and (*b*) peroneus longus to extensor hallucis longus, the shorter distances no doubt account for the more consistent results.

In view of the possible sources of error, the only justifiable conclusion is that regeneration in the intermediate section of the sciatic nerve (just below the knee) occurs at a rate which diminishes from 2 to 1 mm. per day. These values agree with the rates for the radial nerve at and just below the elbow.

SUMMARY

An investigation of the rate of functional regeneration of motor fibers following interruption of conduction in the ulnar and sciatic nerves provided the following results:

1. For the terminal section of the ulnar nerve in the hand, the rate of growth was 0.6 mm. per day after axonotmesis and 0.4 mm. per day after suture.

2. For the section of the sciatic nerve just below the knee, the rate of growth after axonotmesis diminished from 2 to 1 mm. per day.

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University of Melbourne.

NEUROPSYCHIATRIC MANIFESTATIONS DURING THE COURSE OF MALARIA

Experiences in the Mediterranean Theater in World War II

BENJAMIN BOSHES, M.D.
CHICAGO

MALARIA is one of the most widespread and prevalent diseases known to man. The armed forces of the United States encountered this infection in its various forms in many parts of the world. Many thousands of the military personnel were treated successfully for tertian, quartan or malignant tertian infection. In unknown thousands the disease was suppressed by the quinacrine (atabrine)–quinine prophylactic regimen, so that to date there has been no clinical evidence of the infection. It may be expected that with return of the troops to the United States cases of malaria will appear in nonendemic zones as well as in endemic areas. This is because those who have had the disease will have recurrences. Nocht and Mayer [1] pointed out that tertian malaria may recur up to five years in a nonendemic zone and malignant tertian malaria up to two years, and that quartan malaria may lie dormant for years. Furthermore, the previously suppressed disease may become activated. The greater number of patients with symptomatic malaria, as well as the asymptomatic gametocyte carriers, will act as a source of infection for susceptible civilians in areas in which the anopheles mosquito is found. Since malaria is recognized as a disease of protean manifestations, all physicians will have to be on the alert for the plasmodium as the cause of various atypical pyrexial syndromes. Some forms of the disease may even run an afebrile course for some time. Neuropsychiatrists, particularly, will have to watch for the cerebral manifestations.

A review of the literature suggests that malaria with cerebral symptoms is due essentially to Plasmodium falciparum. For example, Nocht and Mayer stated: "With few exceptions, comatose forms occur only in malignant tertian infections." However, in a series of 6,059 cases of malaria in a United States Army general hospital in India,[2] cerebral malaria occurred in 140 cases, or 2.3 per cent. Of the latter group,

Read before the Section on Neurology and Psychiatry at the Ninety-Fifth Annual Session of the American Medical Association, San Francisco, July 4, 1946.

1. Nocht, B., and Mayer, M.: Malaria: A Handbook of Treatment, Parasitology and Prevention, London, John Bale, Sons & Curnow, Ltd., 1937.

2. Fitz-Hugh, T., Jr.; Pepper, D. S., and Hopkins, H. O.: The Cerebral Form of Malaria, Bull. U. S. Army M. Dept., December 1944, no. 83, pp. 39-48.

Plasmodium vivax was the causative organism in 5, as against P. falciparum in 88. Nine cases of the cerebral form were seen in a total of 1,155 cases of malaria in the Mediterranean Theater.[3] In 2 of the 9 cases the causative organism was that of tertian malaria; in 6, P. falciparum. In 1 case no organism was found. The Russians [4] have been much interested in a fulminating form of tertian malaria which attacks children and youths in central Russia. The syndrome is that of an acute, overwhelming infection of the central nervous system, rapidly fatal in a few hours. In 12 of 17 cases examination revealed P. vivax. It becomes imperative, therefore, that one's thinking be flexible as regards the causative organism in malaria. A recent case report from the Veterans Hospital Administration [5] is in point. The patient was psychotic for three weeks in the hospital before the occurrence of chilly sensations and a temperature of 102 F. caused a search for the plasmodium. P. vivax was isolated from the smear, and the patient recovered with specific therapy.

The lesions of cerebral malaria have been well described. Thus, Cerletti [6] pointed out the choking of the blood vessels by the parasites, injury to the vessel walls by the toxins, perivascular changes and formation of new vessels. The leptomeninges show high grade changes. Both the ectodermal and the mesenchymal elements of the brain are involved with ganglion cell disease and hemorrhages into the white substance. Rigdon and Fletcher [7] also described a cellular reaction, with the formation of "malaria nodules" in the cerebrum and the cerebellum. These may be relatively avascular (Dürck's granuloma) or may be associated with hemorrhages. The distribution and nature of the lesions, according to these authors, suggest that the pathologic basis is cerebral anoxia. That the aforementioned lesions are not exclusively the product of P. falciparum may be seen in the report from the King Edward VII Memorial Hospital in Bombay.[8] In many of the cases reported here the disease was diagnosed as meningitis,

3. Horn, H., and Karelitz, S.: Clinical Experience with Malaria at a General Hospital During Summer and Fall of 1943, M. Bull. North Africa Theat. Op. (no. 4) **1**:2-11 (April) 1944.

4. Tarejev, E. M.; Gontaeva, A. A., and Rotenburg, S. S.: Fulminating Type of Tertian Malaria, Sovet. med. (no. 4) **7**:12-14, 1943; abstracted, Trop. Dis. Bull. **41**:257-258 (April) 1944.

5. Singleton, D. E.: Psychosis with Malaria, M. Bull. Vet. Admin. **21**:109-110 (July) 1944.

6. Cerletti, U.: Die histopathologischen Veränderungen der Hirnrinde bei Malaria perniciosa: Beiträge zur Kenntnis der akuten Rindenerkrankungen, in Nissl, F., and Alzheimer, A.: Histologische und histopathologische Arbeiten über die Grosshirnrinde, Jena, G. Fischer, 1910-1911, vol. 4, pp. 169-226.

7. Rigdon, R. H., and Fletcher, D. E.: Lesions in the Brain Associated with Malaria: Pathologic Study on Man and on Experimental Animals, Arch. Neurol. & Psychiat. **53**:191-198 (March) 1945.

(Footnotes continued on next page)

typhoid and pneumonia. In 33 instances the parasite was isolated: P. falciparum, 24 cases; P. vivax, 7 cases; mixed infection, 1 case. Edema, vascular thrombosis and hemorrhages were observed. Granulomas were noted in the brains of patients who did not die quickly. The authors pointed out that the parasitized cells tend to agglutinate and to adhere to the vessel wall; the endothelial cells proliferate, and thrombosis ensues. Diapedesis of red cells and focal necrosis occur. If the patient recovers, the neuroglia proliferate and microglial cells invade the field. The end result is a patch of sclerosis, multiple areas of which may produce considerable alteration of neural function. The authors emphasize that the failure to find parasites in the peripheral blood does not rule out cerebral malaria. In some of their cases smears failed to yield the organism.

With lesions present in all parts of the central nervous system, meninges, blood vessels and parenchyma, the variable presenting syndrome of so-called cerebral malaria may be studied. Certainly, the concept of a "comatose" form only is misleading. In a series of 12 cases of cerebral malaria at a United States naval base hospital, Simpson and Sagebiel [9] described a sudden onset with epileptiform convulsions and coma in 9. Status epilepticus was common. In 4 cases there were signs of meningitis. Acute confusional psychosis developed in 6 cases, with lucid intervals. Pleocytosis, with a count of 30 to 165 cells per cubic millimeter of cerebrospinal fluid, was observed. Others have variously described the clinical syndrome as "cerebral," with symptoms simulating coma, encephalitis, tetanus, epilepsy or meningitis, or as "masked," with symptoms simulating trigeminal neuralgia, migraine, neuritis, aphasia or psychotic episodes.[1] In addition, paralysis of any type, hemianopsias or a bulbar and cerebellar syndrome may occur, the patient thus presenting various neurologic and psychiatric entities. The original diagnosis may well be epilepsy, meningitis, cerebral tumor, encephalitis, cerebrovascular accident or mental disturbance.[10] Arbuse [11]

8. Dhayagude, R. G., and Purandare, N. M.: Autopsy Study of Cerebral Malaria with Special Reference to Malarial Granuloma, Arch. Path. **36**:550-558 (Dec.) 1943; abstracted, Trop. Dis. Bull. **41**:533-535 (July) 1944.

9. Simpson, W. M., and Sagebiel, J. L.: Cerebral Malaria: A Report of Twelve Cases Encountered at U. S. Naval Base Hospital, U. S. Nav. M. Bull. **41**:1596-1602 (Nov.) 1943.

10. Kneedler, W. H.: Symposium on Tropical Medicine: Malignant and Atypical Malaria, Clinics **2**:809-827 (Dec.) 1943. Brill, N. Q., and Pellicano, V. L.: Estivoautumnal Malaria with Frontal Lobe Syndrome, J. A. M. A. **121**: 1150-1152 (April 3) 1943. McGinn, S., and Carmody, J. T. B.: Cerebral Symptoms in Malaria, U. S. Nav. M. Bull. **43**:1157-1162 (Dec.) 1944. Hyman, A. S.: Clinical Masquerades of Malaria: Observations in the South Pacific Combat Areas, ibid. **45**: 287-303 (Aug.) 1945. Eckstein, A.: Malaria und Zentralnervensystem im Kindesalter, Ann. pædiat. **168**:65-96, 1942.

11. Arbuse, D. I.: Neuropsychiatric Manifestations in Malaria, U. S. Nav. M. Bull. **45**:304-309 (Aug.) 1945.

pointed out that, in addition to the focal lesions in the substance of the central nervous system, neuritis of the optic nerve and the abducens, facial, ulnar and peroneal nerves, as well as the brachial plexus, has been observed. Paraplegias due to involvement of the spinal cord have been seen. Arbuse raised the question of the validity of considering polyneuritis a complication of malaria, since the latter occurs in areas where beriberi is prevalent. He expressed the opinion that latent beriberi may be activated by malaria. He classified the neuropsychiatric manifestations as (1) those presenting meningitis, with slight focal or generalized neurologic signs; (2) those with definite localizing significance, such as apoplectic phenomena, coma and convulsions, and (3) those referable to the spinal cord and peripheral nerve. Horn and Karelitz,[8] describing cases from the Mediterranean Theater, raised the question whether their 4 patients with herpes zoster and the 3 with meningoencephalitis did not have an intercurrent virus infection activated by the malaria. However, the known pathologic lesions of cerebral malaria would be consonant with a clinical picture of meningoencephalitis; and herpetic lesions, particularly the labial form, were the rule, even in uncomplicated cases. It is unnecessary, therefore, to invoke an etiologic agent other than the plasmodium and its by-products.

In assessing some of the psychotic reactions incident to malaria, the role of the medication must be determined. This is not always possible, because many patients, particularly children, become disturbed during protracted periods of high fever. In addition, the toxic-exhaustive effects of repeated, or even of a single, attack of malaria are not to be denied. However, there are a sufficient number of cases of toxic responses to quinacrine with psychotic manifestations to make one investigate the subject. In a chronic experiment in cats, Pick and Hunter [12] were able to show that quinacrine produced a central depressant action, the degree depending on the content of drug in the brain, and not in the blood. Scudi and his co-workers [13] demonstrated that experimentally quinacrine produces irritation of the gastrointestinal tract, with diarrhea, hemoconcentration and loss of blood chlorides and blood bicarbonates. Large doses produce necrosis of the liver. The toxic effect can be increased by fasting the animals or prevented by feeding them a high protein and low fat diet. Thompson [14] treated

12. Pick, E. P., and Hunter, J.: Action of Atabrine on Electrocortico Potentials, J. Pharmacol. & Exper. Therap. **80**:354-361 (April) 1944.

13. Scudi, J. V.; Jelinek, V. C., and Kuna, S.: Biochemical Aspects of the Toxicity of Atabrine: Acute Effects of Massive Doses in Rat, J. Pharmacol. & Exper. Therap. **80**:144-149 (Feb.) 1944. Scudi, J. V., and Hamlin, M. T.: Biochemical Aspects of the Toxicity of Atabrine: II. Influence of Diet upon Effects Produced by Repeated Doses of the Drug, ibid. **80**:150-159 (Feb.) 1944.

14. Thompson, J. H.: Large Initial Doses of Atabrine in the Treatment of Benign Tertian Malaria, J. Trop. Med. **47**:61-64 (Dec.-Jan.) 1944-1945.

100 patients with relapses and latent benign tertian malaria. In patients given an initial dose of 0.6 Gm. of quinacrine hydrochloride, then 0.2 Gm. three times a day for six doses, then 0.1 Gm. three times a day for one week, no toxic symptoms developed. Four of 8 patients taking 1.0 Gm. had nausea. One man had "strange thoughts running through his head," which cleared up as the disease subsided. Lerro [15] reported 2 cases of neuropsychiatric complications which disappeared immediately when the drug was discontinued. This has been the experience of many others.[16] Bispham [17] studied 49,681 patients receiving quinacrine therapy. Of the 38 patients showing toxic symptoms of all types, varying from gastrointestinal disturbances and simple headache to severe psychosis, all had prompt clearing of their symptoms as soon as the drug was stopped. In evaluating reports from the Malay States, India and China, Nocht and Mayer [1] (page 52) pointed out the extremely low incidence of neuropsychiatric reactions, e. g., 2 cases of temporary delirium in 750 cases and 2 cases of depression in 1,200 cases. All workers describing large numbers of cases are agreed on the very low frequency of toxic cerebral reactions and the prompt reversibility when the drug is removed.

These observations are in keeping with the experience of my colleagues and myself. We were in contact with tens of thousands of soldiers taking quinacrine as suppressive treatment, 0.4 Gm. per week. Large numbers of patients over a period of almost three years were treated for malaria in the general hospital with which we were associated, but not a single case of quinacrine psychosis was encountered. Our introduction to quinacrine prophylaxis during the final phases of the Tunisian campaign, in the spring of 1943, was dramatic. The incidence of incapacitating vomiting and diarrhea was very high for three or four days. Patients and medical personnel were equally affected. The performance was not repeated in 1944 or 1945 when quinacrine therapy was resumed. Why the toxic response to the 1943 batch of quinacrine was so widespread has never been explained. Many patients turned a yellow-green from intake of the drug, but there was no concomitant toxic effect. The color disappeared on discontinuance of the drug.

In the Mediterranean Theater the incidence of cerebral malaria was comparatively low. The frequency of infections with P. falciparum fell off after the North African and Sicilian campaigns. In the Horn and

15. Lerro, S. J.: Report of Two Cases of Toxicity to Atabrine, Mil. Surgeon **89**:668-670 (Oct.) 1941.

16. Mental Symptoms Following the Use of Atabrine, editorial, J. A. M. A. **121**:765 (March 6) 1943. Ayala, F., and Bravo, G.: Psychosis Observed in the Treatment of Malaria with Atepe, Rev. clín. espan. **7**:70-72 (Oct. 15) 1942.

17. Bispham, W. N.: Toxic Reactions Following the Use of Atabrine in Malaria, Am. J. Trop. Med. **21**:455-459 (May) 1941.

Karelitz [8] series of 1,155 cases, in the summer of 1943, 39.1 per cent were of the benign tertian variety and 33.7 per cent of the malignant type. The cases came from Sicily and the Eastern Base Sector of the North-African Theater, the Tunis-Bizerte Sector. Estivoautumnal malaria was exceedingly uncommon in Italy. Golz [18] pointed out that in 75 per cent of the cases reported between November 1942 and March 1945 the malaria was of the P. vivax variety and in 10 per cent of the P. falciparum group, and that the latter were a product of the early days of Tunisia and Sicily. These data reflect our experience, despite the fact that malaria was the greatest single cause of hospitalization in the Theater, and that the malaria rate often exceeded the figure for battle casualties by as much as 20 per cent.

The cases that were presented to the neuropsychiatrist, especially when the Italian campaign was under way, were the bizarre, the atypical—in short, the type of case I am trying to point out as a "Stateside" challenge. The psychiatrist was often called to see a patient with a bursting headache, severe retro-orbital pain and backache. No focal or meningeal signs could be elicited, but the advent of a typical or atypical febrile course would lead to a series of "malaria slides" being made, with the result that the diagnosis was readily established. However, if the patient entered with a diagnosis of "epilepsy," "suspected cerebellopontile angle tumor" or "psychosis unclassified" and he was afebrile, the problem was more difficult. The routine practice of making a thick and a thin blood smear for every patient who became febrile, no matter how mildly, helped to establish the presence of malaria. The importance of obtaining repeated smears, thick and thin, at several intervals of the day, preferably several hours after the paroxysm, is emphasized.

The vagaries of symptoms in an atypical case of cerebral malaria are seen in the following presentation:

History.—L. J. B., a staff sergeant aged 26, fighter squadron in Italy, became ill Oct. 6, 1944, with nausea and some vomiting. That afternoon he began to "shake." No further history could be elicited. The temperature was 97 F., the pulse rate 104 and the respiratory rate 24. There were no abnormal findings, but the patient was apprehensive, resistive and incoherent. The battalion surgeon who had sent the patient into the station hospital, on Oct. 7, expressed the opinion that the patient might have malaria because the temperature was 100.2 F. at the time of onset. Two smears were negative for malaria.

The patient was semicomatose on October 8. Lumbar puncture done on that day revealed elevated pressure, with 84 cells per cubic millimeter, 30 polymorphonuclear leukocytes and 54 lymphocytes. The medical officer considered the diagnosis of choriolymphocytic meningitis or encephalitis. On October 11 the patient had four generalized convulsions.

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18. Golz, H. H.: The Diagnosis and Treatment of Malaria, M. Bull. Mediterranean Theat. Op. **3**:103-111 (April) 1945.

Examination.—He was transferred to our general hospital with the diagnosis of "epilepsy" and was received on October 11, in deep coma. There was considerable motor unrest but no movements of the limbs on the right side. Examination was difficult but revealed ankle clonus bilaterally, Babinski and Oppenheim signs and absence of abdominal reflexes. The right side of the face did not move as well as the left. There was a slight internal squint of the right eye. Pendular nystagmus was present on looking ahead. This changed to a definite slow vestibular type on looking to the right. Conjugate movements of the eyeballs were preserved. The pupils dilated to darkness and reacted poorly to light. The fundi were normal. The patient did not respond to painful stimuli. Definite nuchal indications of meningitis, with a direct Brudzinski sign and a bilateral Kernig sign, were present. The temperature was 102.2 F., the pulse rate 96, the respiratory rate 22 and the blood pressure 126 systolic and 80 diastolic.

The picture was that of acute meningoencephalitis. How many of the focal signs were due to the illness per se and how many were the product of the postconvulsive state could not be determined then.

Spinal puncture yielded clear fluid, under a pressure of 280 mm. of water, with normal dynamics. Examination revealed 4 white cells (lymphocytes) per

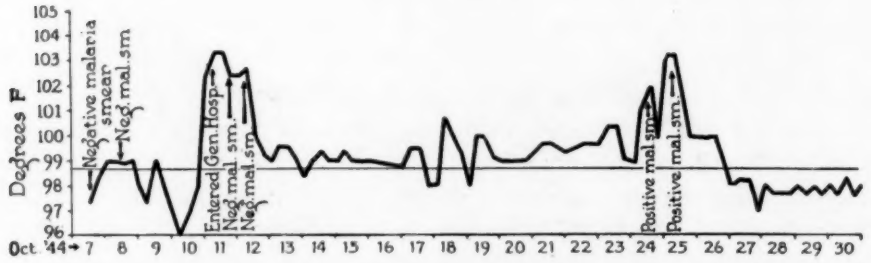

Fig. 1.—Temperature chart in a case of malaria with cerebral complications due to Plasmodium vivax.

cubic millimeter; 100 mg. of sugar and 733 mg. of chlorides, per hundred cubic centimeters, and a negative reaction for globulin. The total protein was 22 mg. per hundred cubic centimeters. The Kahn reaction was negative. The colloidal gold curve was 1111000000. A subsequent smear, culture and pellicle test all failed to reveal the parasites.

Course in Hospital.—The temperature dropped to normal on October 12. The patient responded to questions but was confused much of the time. Neurologic signs persisted.

October 13: Spinal puncture revealed that the spinal fluid was clear and under a pressure of 260 mm. of water. The pressure dropped to 70 mm. of water after removal of 30 cc. of fluid. Examination revealed 5 white blood cells (lymphocytes) per cubic millimeter, and 62 mg. of sugar (simultaneous blood sugar level, 84 mg.) and 759 mg. of chlorides per hundred cubic centimeters. The reaction for globulin was negative, and the total protein was 24 mg. per hundred cubic centimeters. Smear and subsequent culture did not reveal parasites. That day a generalized convulsion occurred and then a jacksonian fit on the right side; an attack of "status epilepticus" was aborted with intravenous injection of sodium amytal.

October 14: Right homonymous hemianopsia, transient, was suspected; there were periods of delirium and hallucinations. The patient was afebrile.

October 16: Two attacks of furor, epileptic equivalents, occurred.

October 17: The patient showed right homonymous hemianopsia (fig. 2 A). There was no astereognosis. A tendency toward perseveration was evident. Meningeal signs persisted.

October 17 to 24: The condition was essentially unchanged. The patient was somewhat confused. The right hemianopsia persisted (fig. 2 *B*).

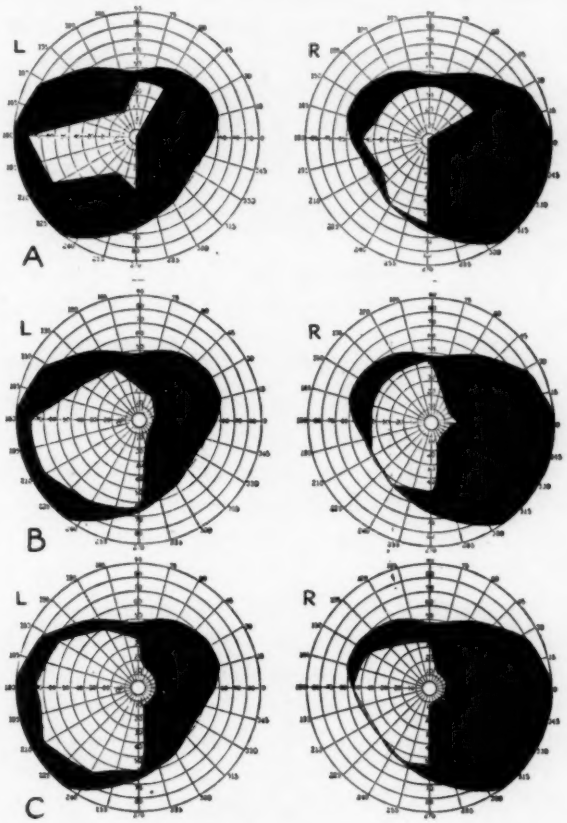

Fig. 2.—Visual fields in a case of malaria with cerebral complications due to Plasmodium vivax. *A*, fields on Oct. 17, 1944; *B*, fields on October 22, and, *C*, fields on October 30.

October 24: The temperature rose to 101.8 F. A smear of the blood revealed P. vivax.

October 25: The temperature rose to 103.4 F. during the morning. A second slide showed malarial parasites (P. vivax). Administration of quinine sulfate, 15 grains (0.975 Gm.) three times a day by mouth, was started.

Studies of the Blood.—Four smears made prior to October 24 had been negative for malaria parasites, and the patient had been afebrile for days when the organism was found. The white blood cell counts were as follows: October 7: 12,350 (neutrophils 80 per cent, lymphocytes 20 per cent); October 8: 5,300 (neutrophils 74 per cent, lymphocytes 26 per cent); October 11: 20,600

(neutrophils 89 per cent, lymphocytes 11 per cent); October 16: 4,300 (neutrophils 46 per cent, lymphocytes 54 per cent); October 25: 11,500 (neutrophils 64 per cent, lymphocytes 36 per cent).

Serologic Studies: The Kahn reaction of the blood was positive on October 11; the Kahn and Wassermann reactions of the blood were negative on October 17; all Kahn reactions of the spinal fluid were negative.

Special Laboratory Studies (October 25).—The blood bromide level was 75 mg. per hundred cubic centimeters.

Spinal puncture revealed a pressure of 200 mm. of water; 2 white blood cells (lymphocytes) per cubic millimeter, and 56 mg. of sugar, 685 mg. of chlorides and 26 mg. of total protein, per hundred cubic centimeters. The colloidal gold curve was 111100000.

Subsequent Course.—The patient was afebrile on October 26 and has been so since. He was normal mentally. All neurologic signs cleared up except the right homonymous field defect, which was still present when he was transferred to another general hospital, on Nov. 1, 1944.

Diagnosis.—The diagnosis was severe tertian malaria, with meningoencephalitic manifestations.

Studies of the blood and spinal fluid at the Army virus laboratory revealed that there was no neutralization of any of the known neurotropic viruses.

COMMENT

This man's illness started with a chill and low grade fever. Malaria was suspected, but two smears were negative for the parasites. The rapid onset of symptoms of meningoencephalitis with changes in the spinal fluid indicative of meningitis raised the question of a virus infection. However, the occurrence of the convulsions caused the diagnosis to be changed to "epilepsy." The presence of coma, a brain stem syndrome, in the presence of a temperature of 102.2 F. and meningeal signs ruled against the diagnosis of epilepsy. A normal cerebrospinal fluid and an afebrile course for many days did not help in the diagnosis. Two more smears were negative for malarial parasites. Evidence of transient focal disturbances in the brain was always present. On October 13 there occurred a generalized convulsion and then jacksonian fits on the right side. The next day transient right homonymous hemianopsia appeared, with periods of delirium and hallucinations. Epileptic equivalents, furor states, made an appearance, and, finally on October 17, a right homonymous hemianopsia became evident and persisted. All but the last symptom cleared up promptly when he was placed under quinine therapy. As often occurs in these cases, there was a transient positive reaction of the blood to the Kahn test. P. vivax was isolated on two occasions, and virus studies of the blood and the spinal fluid drawn during the acute illness gave negative results. The case was therefore unquestionably one of malarial meningoencephalitis with multiple neuropsychiatric manifestations.

Treatment was in accordance with current practice. Since the patient could swallow, he was given quinine by mouth. Quinacrine

would have worked as well. Had he been in deep coma and severely ill, we should have administered 0.6 Gm. (10 grains) of quinine dihydrochloride intravenously in 200 to 300 cc. of isotonic solution of sodium chloride, injecting it very slowly. This procedure could be repeated in three to four hours, but it was the policy of the Army [19] to anticipate the need by giving intramuscular injections of quinacrine dihydrochloride, 0.2 Gm. (3 grains) in 5 cc. of sterile water in each buttock, a total of 0.4 Gm. (6 grains). As soon as the patient was conscious, the oral administration of quinacrine or quinine could be started.

The usual supportive measures—fluids and anticonvulsants, such as sodium amytal given intravenously—were utilized. (Patients in medical shock or with low blood counts were given transfusions, liver extract or iron, as needed.) After the patient was clinically well, the usual suppressive measures were again instituted. The patient had failed to take the prophylactic dose of quinacrine dihydrochloride for several weeks before he became ill with the infection.

CONCLUSIONS

1. Malaria was a common disease in the American armed forces in the Mediterranean Theater of Operations.

2. Neuropsychiatric complications simulating meningitis, encephalitis, epilepsy, cerebral tumor, vascular lesions and psychiatric disorders were encountered.

3. "Cerebral" forms of malaria were not limited to the disease caused by P. falciparum, but P. vivax and mixed infections could produce these pictures.

4. Quinacrine (atabrine) proved to be an effective nontoxic suppressive and active antimalarial drug.

ADDENDUM.—Since this article was written, two papers have appeared, one [20] describing toxic psychoses associated with the administration of quinacrine, and another [21] setting forth the histopathologic changes in cerebral malaria as related to psychotic sequelae.

30 North Michigan Avenue.

ABSTRACT OF DISCUSSION

DR. W. MCD. HAMMON, Berkeley, Calif.: This presentation is timely. I wish merely to emphasize that a great variety of unusual manifestations due to relapsing malaria may occur among returned servicemen during the next few years.

19. Treatment of Clinical Malaria and Malarial Parasitemia, United States War Department, Technical Bulletin (TB Med 72), Washington, D. C., Government Printing Office, July 10, 1944.

20. Sheppeck, M. L., and Wexberg, L. E.: Toxic Psychoses Associated with Administration of Quinacrine, Arch. Neurol. & Psychiat. **55**:489-510 (May) 1946.

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Fortunately, there will be far fewer relapses of malaria due to P. falciparum, which is more likely to be associated with bizarre localized lesions, cerebral as well as others, than malaria of the P. vivax type; but, as Dr. Boshes has pointed out, the latter type is not always free from such complications.

Malaria from the Pacific areas, which I was fortunate enough to see both here in San Francisco and on Okinawa, presented a picture similar to that in the Mediterranean area. Severe psychoses; mild psychoneuroses of both short and long duration, and motor disturbances, including convulsions, encephalitis and meningismus, were among the manifestations noted. The occurrence of any of these symptoms in a veteran should raise the question of malaria in the mind of the physician, and one or two negative blood smears, particularly if examined by inexperienced technicians, should not eliminate that possibility. One should not be misled by the patient's statement that he has never had malaria and has now gone without quinacrine for several months, or even a year. Although most infected persons in whom the P. vivax parasites have been suppressed by quinacrine exhibit clinical malaria within a few weeks after stopping the drug, much longer intervals are by no means rare. Neither is it safe to generalize and to conclude that since a patient has not had a relapse in six or eight months he is cured.

I have observed several cases of acute malaria here, in the Pacific and in Africa in which the illness was first diagnosed as virus encephalitis, poliomyelitis or trypanosomiasis. Two such infections may exist concurrently, and the malaria parasites demonstrated may be only a manifestation of a latent, inactive, phase or of a clinical "bout" precipitated by the primary condition. Although I believe it unlikely, one cannot deny that the illness in the case presented by Dr. Boshes may have begun as a self-limited encephalitis of unknown origin, and not as malaria. At this stage of the disease malaria parasites were not observed. As spontaneous recovery was about to occur, the patient had an attack of malaria, accounting for the late rise in temperature and the observed parasitemia, which, in turn, yielded to specific therapy. The first infection could have accounted for the "break through" of the malaria. I recall the case of a paralyzed child in Costa Rica which was presented to me as one of cerebral malaria with permanent residual manifestations. The proof offered was that parasites were demonstrated and that the temperature fell after administration of quinine. The residual symptoms, however, were asymmetric flaccid paralyses, not unlike those of poliomyelitis.

I do not mention these cases to throw doubt on the diagnosis in the case presented, which is probably correct. I desire simply to emphasize that cerebral malaria can mimic closely other diseases. Physicians in this country think first, of course, of more common domestic disturbances, and physicians in the tropics think first of malaria and may miss other diagnoses. Since highly effective therapeutic agents are available for malaria, one must not fail to consider their use in appropriate cases.

Dr. Meyer A. Zeligs, Cincinnati: The importance of properly recognizing the protean manifestations of malaria, which during the war was primarily a problem of military medicine, is now a matter of concern to all physicians. When it is realized that tens of thousands of war veterans are now at large throughout the country, the social and medical aspects of this disease rank among the foremost postwar problems.

Dr. Boshes' experiences with this disease in the Mediterranean Theater would indicate that the central nervous system may be seriously involved even in cases of the benign tertian form. He has emphasized that the occurrence of cerebral manifestations during the course of the disease is not limited exclusively to the malignant tertian (P. falciparum) form of malaria and has pointed out the remarkable frequency of cerebral involvement in patients with benign tertian (P. vivax) infections. Fortunately, this has not been my experience. Out of a total of 2,500 Marines returned from the South Pacific with benign tertian malaria who were studied at Klamath Falls, Ore., for periods varying from three months to as long as a year, my colleagues and I saw no cerebral manifestations at any time. I wonder, therefore, whether the parasite in the cases which Dr. Boshes saw in the Mediterranean Theater may not have been of a different strain from that in the South Pacific Theater. Or is it possible that the rigors and physical fatigue associated with the combat situation so altered the bodily economy as to allow the parasites of benign malaria to produce what is ordinarily regarded as malignant manifestations? It is interesting in this regard that in our studies at Klamath Falls, we found that many malarial patients who had just been returned from combat with the diagnosis of "postmalarial asthenia," when carefully and deliberately appraised, were shown to have concomitant infections, such as amebiasis or hookworm, and that when these infections were specifically treated the "asthenic" state cleared dramatically. Many men with combat neurosis were also considered to be asthenic because of their recurrent malaria. With proper psychotherapy, however, and an appropriate rehabilitative program, these patients recovered from their asthenia most gratifyingly.

Dr. Boshes mentioned a distressing symptom—headache. We found that 15 to 20 per cent of men with a history of recurrent malaria were subject to frequent bouts of mild to severe headache. In fact, we soon realized that this symptom in itself was one of the most disturbing features of the interval phase of this disease. This "malarial headache" was most often present on arising in the morning and usually improved after the patient had been up a few hours. An almost characteristic feature of patients with attacks of malarial headache was their intolerance to physical exertion and exposure to the sun. This almost invariably brought about a severe headache. These men did not obtain relief with the usual remedies for headache. Salicylates, barbiturates, and even codeine, were found to be of no value in relieving this type of headache. On the assumption that the headache was the result of clogging of cerebral capillaries with parasite-laden red blood cells, with resulting venular congestion and cerebral anoxia, I tried using a vasodilating drug and found that the headache of many of these patients was relieved with 100 mg. of nicotinic acid taken orally.

I should like to ask Dr. Boshes how long the soldiers observed with cerebral manifestations had been in combat and what was the incidence of combat or operational fatigue in the entire series.

Dr. Cullen Ward Irish, Los Angeles: Reports of cerebral malaria with localized manifestations have been few. Dr. Boshes' presentation adds to previous meager descriptions of such instances, of which there is a sufficient number, however, to emphasize the fact that cerebral malaria may assume any known form of disease of the nervous system.

I had the opportunity of observing a patient, a soldier aged 21, with residual symptoms of cerebellar involvement following malarial infection. This patient was in apparent good health until mid-January 1944, when he was admitted to

an Army hospital in the South Pacific. He was stuporous the first two days, but after treatment with quinine and quinacrine he recovered progressively and was discharged to duty Feb. 15, 1944. He then became increasingly weak, had much difficulty in standing and walking and suffered from persistent headache. After three days on duty he is said to have collapsed and was rehospitalized. The next day the gait was broad based and lurching, with flail-like movements of the legs, hyperreflexia and choking of the right optic disk.

On his transfer to the Army general hospital in this country, neurologic examinations revealed a broad-based, ataxic gait with gross tremors of both legs, so that the gait had a dancing quality. The patient fell to the left and backward in the Romberg position. No speech disturbance was present, but fine movements were impaired in both hands. A slight intention tremor occurred in coordination tests with the upper extremities, and there were severe tremor and ataxia in the lower extremities. Little improvement or change occurred.

In this case, it is apparent that the patient had acute cerebral involvement, manifested chiefly by stupor at the onset. A month later progressive weakness and tremor, particularly of the incoordination type, with persistent headache indicated the recurrence of intracranial malarial involvement. The caloric tests indicated that permanent damage had occurred in the pathways for equilibration. The rest of the symptoms were localizable to the cerebellum, where irreversible degeneration from foci of encephalomalacia had occurred.

Knowledge of such complications of malaria must be more widely disseminated. Recognition of the possibility that cerebral symptoms may be due to malaria, irrespective of knowledge of such exposure or of the region in which the patient may present himself, may be invaluable in saving life, since early proper therapeusis is commonly effectual.

Dr. Benjamin Boshes, Chicago: I am much interested in Dr. Hammon's concept that previous infection, such as virus infection, may break down the barrier and permit the plasmodium to break through and establish itself in the central nervous system. Symptoms may be divided into two types: meningeal symptoms and symptoms due to direct involvement of the blood vessels. I can conceive how a previous virus infection might break down the meningeal component of the barrier, with the result that the cerebrospinal fluid would show evidence of invasion. However, it appears to me that in our case the symptoms were due to vascular involvement, since the course of the localization, the jacksonian fits and the homonymous hemianopsia indicated that branches of the middle cerebral artery were involved. I might admit that when I first examined this patient my thinking was that of a civilian. I thought of virus infection and sent cerebrospinal fluid to the Army virus laboratory in Washington, D. C. I drew four samples of fluid, taking them in the afebrile and the febrile period. Admittedly, not many viruses can be identified specifically; however, all virus neutralization tests gave negative results.

The role of effort in relapses is important. Patients with hepatitis have prompt relapse on effort, and such patients were being returned to us as "psychoneurotic." We learned to give them an exercise tolerance test and put them through an obstacle course before sending them back to combat. The same was true with "malarial" patients. We learned to put them through exercise and obstacle course and found that occasionally a patient with true malaria would have a relapse as soon as the soldier became active. I do not think that physical

exertion played an active role in the present case, that of a sergeant in the ground forces of the air corps.

We saw more cases of malaria and "malarial neurasthenia" among foot soldiers. I think this is related to the more frequent exposure of foot soldiers to malaria in the marshes of Sicily and Italy.

The intolerance of heat brings up an important point. An Italian physician in Naples told me that the Italian army had had no malaria during the Ethiopian campaign, but that there had been many cases of "heat stroke." I finally pinned him down to what he meant by "heat stroke." He admitted that there was so much malaria in the Italian army during the Abyssinian campaign and among the troops in Eritrea and elsewhere that Mussolini issued an edict that no diagnosis of malaria be made; henceforth, it should be called "heat stroke."

ORIGIN OF TUMORS OF THE MIDBRAIN

J. M. FRIEDMAN, M.D.*
NEW YORK
AND
L. GREENSTEIN, M.D.
BROOKLYN

ALTHOUGH tumors of the midbrain have been repeatedly described, the emphasis has invariably been placed on the clinical manifestations of such lesions. The tumors already recorded include many forms: A large number were in the nature of pineal growths; others had their origin in adjacent areas of the brain and only by contiguity and direct extension involved the midbrain. Globus and Silbert [1] clarified the histologic characteristics of a large quota of tumors of the midbrain of a somewhat varied appearance by identifying them as pinealomas, establishing this unity on an embryologic basis. They set these neoplasms apart from other neuroectodermal tumors occurring in that region. Such tumors, with their primary site of origin in the midbrain, are few. Bailey and Cushing [2] encountered 18 in the brain stem (pons and midbrain) in a total of over 1,000 gliomas. None of these was classified or described. Tooth,[3] in a review of 500 cases of cerebral tumor, found 26 in which the midbrain was involved; in 8 of these the diagnosis was verified at autopsy, 4 of the tumors being classified as gliomas, 1 as a sarcoma, 2 as tuberculomas and 1 as a cyst. Several other authors (Marburg and Ranzi,[4] Olivecrona [5] and Dowman and Smith [6]), reviewing large series of brain tumors, included no instances

*Isadore Abramson Memorial Fellow in Neuropathology.

From the Neuropathologic Division of the Laboratories of the Mount Sinai Hospital.

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3. Tooth, H. H.: Some Observations on the Growth and Survival Period of Intracranial Tumors Based on the Records of Five Hundred Cases, with Special Reference to the Pathology of the Gliomata, Brain **35**:11, 1912.

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of tumor of the midbrain. In a survey of cerebral tumors collected over a period of twenty years in the neuropathologic laboratory of the Mount Sinai Hospital, only 3 neoplasms were found to have had their true origin in the midbrain and confined to it. One of these was a hemangioma, and the other 2, to be reported here, were neuroectodermal tumors.

REPORT OF CASES

CASE 1.—*History.*—J. R., a man aged 29, ten days before admission to the Mount Sinai Hospital was suddenly seized with chills and severe pain in the left side of the back of his head. Stiffness of the neck followed, and five days later urinary incontinence developed. The next day he became delirious and soon

Fig. 1 (case 1).—Cross section of the midbrain, showing tumor within the aqueduct of Sylvius.

lapsed into a drowsy, dull state. During the following three days he was restless and unable to sleep. On the ninth day of his illness he passed through several generalized convulsive seizures with a short period of unconsciousness, followed by repeated vomiting. Throughout his illness there was no elevation of temperature.

Examination.—The patient appeared acutely ill and irrational, with slow, thick speech. The pupils were miotic, irregular and fixed to light and in accommodation. There were paralysis of convergence, fine nystagmoid twitchings on lateral fixation and slight skew deviation of the eyes. The eyelids showed bilateral ptosis. There were general muscular weakness, with hyperactive deep reflexes, and stiffness of the neck; a Kernig sign of moderate intensity and a Babinski sign were present bilaterally. Lumbar puncture yielded clear cerebrospinal fluid under an initial pressure of 168 mm. of water. The fluid contained 3 cells per cubic millimeter, and the Pandy reaction was negative.

Course of Illness.—Acute epidemic encephalitis was considered as the probable diagnosis. The patient's condition grew worse; he became stuporous and died on the ninth day in the hospital.

Gross Necropsy Observations.—There was moderate congestion of the vessels of the cortex. In retracting the frontal lobes, numerous adhesions were noticed in the perichiasmatic region. The floor of the third ventricle was greatly thinned and translucent, as a result of the internal hydrocephalus. The optic tracts appeared to be displaced laterally by the bulging of the tuber cinereum. A section through the midbrain displayed an obstruction in the aqueduct just caudal to the junction with the third ventricle. It appeared to have been caused by a small

Fig. 2 (case 1).—Section of the tumor, showing its relationship to the subependymal cell plate in the floor of the aqueduct.

round body containing two or three yellowish cystic areas (fig. 1). The aqueduct was greatly dilated rostrad to the obstruction and slightly dilated below it. At the point of obstruction it seemed to be completely obliterated, and its site marked an area of yellowish discoloration outlining approximately the extent of the periventricular gray matter. Viewed from the caudal aspect, the free and rounded surface of the tumor projected freely into the anterior part of the fourth ventricle. The ventricular system rostrad to the aqueduct was considerably enlarged, the internal hydrocephalus being symmetric. The interventricular foramens were large and provided a wide intercommunication between the two lateral ventricles, as well as with each other.

Microscopic Observations.—The tumor tissue, sections of which were stained with hematoxylin and eosin, was densely cellular and moderately well vascularized. There were encountered a few large cystlike spaces, surrounded by somewhat loose tissue. Within these spaces were compound granular cells. On tracing the periphery of the tumor mass one found that the growth was intimately related to the subependymal tissue, suggesting the probability that the neoplasm was an outgrowth of the subependymal cell plate in the region of the floor of the aqueduct, reducing the aqueduct to a narrow slit (fig. 2). Except for bare areas and the site of fusion with the tumor, the aqueduct retained a fairly normal ependymal lining. Uninterrupted ependyma extended also over a portion of the protruding tumor mass. In one segment the ependymal lining was thickened and displayed several cell layers, which gradually blended with the neoplastic tissue (fig. 3). At

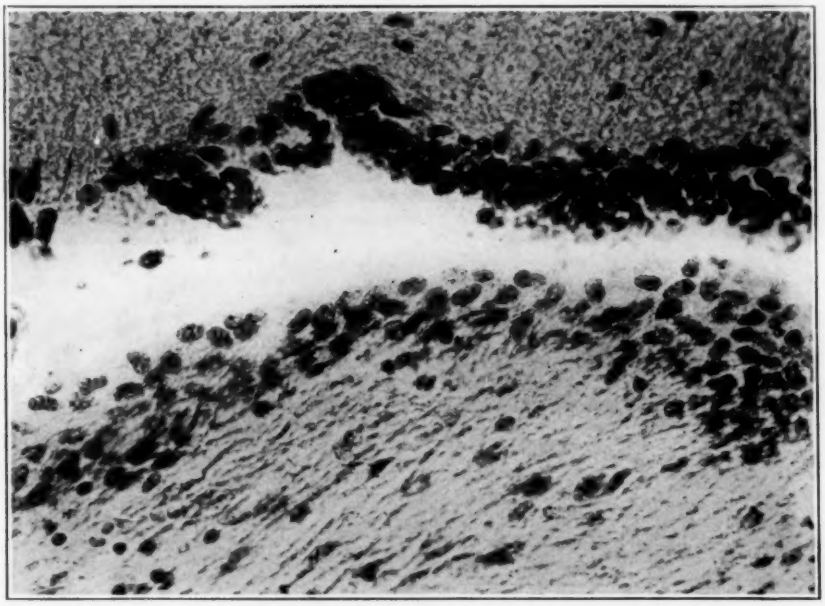

Fig. 3 (case 1).—Section of the tissue, showing stratified ependymal epithelium lining the surface of the tumor and the aqueduct.

points of contact of the tumor with the wall of the aqueduct ependymal lining separated it from the uninvolved brain tissue (fig. 4).

The dominant cell in the tumor was a long, fusiform bipolar cell, giving rise to rather long fibrous extensions. These fibers were arranged in broad, streaming bundles, running in various directions. In addition, there were stellate glial elements, which showed several transitional stages toward the elongated, spindle-shaped type. In some segregated areas there were multinuclear, but rather moderate-sized, cells of the spongioblastic giant cell variety. A few large neuroblasts were scattered among the other tumor cells, as were a few mitotic figures.

Many of the vessels showed perivascular infiltration with small round cells. Silver preparations revealed a network of fine argentophil fibers within the tumor. These fibers were directly continuous with the adventitial reticular framework of the blood vessels. The gray substance of the tegmentum in the proximity of the tumor contained degenerating nerve cells, showing the picture of tigrolysis.

Among the cells of the oculomotor nucleus was an occasional binucleated motor cell (fig. 5).

In serial cross sections of the tumor stained with hematoxylin and eosin, remnants of ependymal cysts were seen in the depths of the basal plate of the aqueduct (fig. 6).

Comment.—This tumor presented a significant feature in its topographic relation to the subependymal cell plate surrounding the aqueduct. The tumor gave the impression of being well demarcated from the surrounding tissue, thus showing an expansive, compressing type of growth rather than an infiltrating, invasive one. The expansion was directed toward the aqueductal space. At its base the tumor extended nowhere

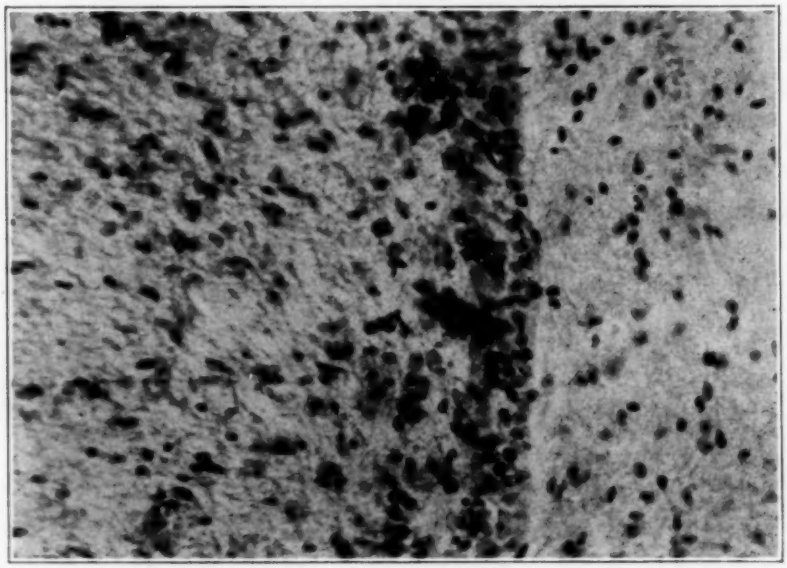

Fig. 4 (case 1).—Section of the tumor, showing a band of cells marking the separation between tumor tissue and the adjacent, apparently unaltered, part of the brain stem.

beyond the limits of subependymal cell plate. In this zone the neoplastic cells gradually blended through transitional cell forms with the normal elements of the subependymal cell plate. The topographic relations of this tumor and certain constant embryonic changes observed by Turkewitsch [7] and Hochstetter [8] in the developing aqueduct point to a probable source of this primary tumor of the midbrain.

In the course of an extensive search, suggested by Dr. Globus, for the probable embryonic factors bearing on the development of primary

7. Turkewitsch, N.: Die Entwicklung des Aqueductus cerebri des Menschen, Morphol. Jahrb. **76**:421, 1935.

8. Hochstetter, F.: Beiträge zur Entwicklungsgeschichte des menschlichen Gehirns, Vienna, Franz Deuticke, 1919, pt. 2.

neoplasms of the midbrain, there were encountered the highly significant and suggestive observations of Turkewitsch [7] and Hochstetter.[8] In median longitudinal sections of the midbrain of human fetuses of from 4 to 8 months, Turkewitsch observed ependymal folds covering the surface of the tegmental colliculi and projecting into the passage of the midbrain (fig. 7). In their ultimate obliteration by fusion, ependymal

Fig. 5 (case 1).—Section of the tumor, showing a vessel infiltrated with dark-staining cellular elements and streaming fusiform cells.

residues were often observed to persist. Hochstetter, on the other hand, in cross sections of human embryos of 3 months, observed symmetrically located areas denuded of ependymal epithelium at the junction of the caudal sac of the midbrain with the cavity of the midbrain. The bare surfaces were covered by a large number of round cells, and in the exposed matrix there were usually encountered subependymal cell groups.

The persistence of embryonic elements in the basal plate of the aqueduct at its junction with the caudal sac of the midbrain, as observed by Turkewitsch, is significant, as these residual nests constitute a

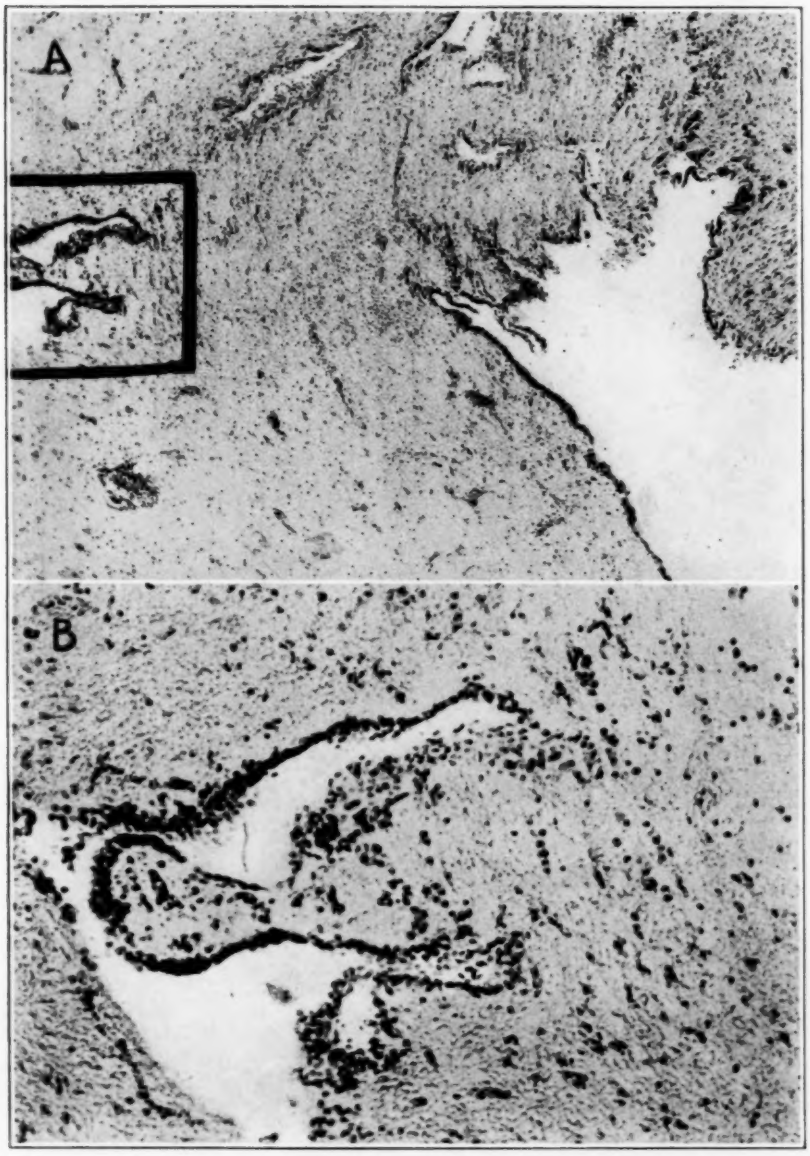

Fig. 6 (case 1).—*A*, serial section of tumor, showing ependymal cyst at the periphery of the tumor (in the rectangle). *B*, higher magnification of the ependymal cyst.

by-product of an excessive growth of ependymal folds which normally undergo complete involution and serve as a nucleus of neoplastic forma-

tion. The persistence of the bare areas in the developing aqueduct, as observed by Hochstetter, is significant in that, the restraining influence of a limiting membrane being absent, any blastomatous formation aris-

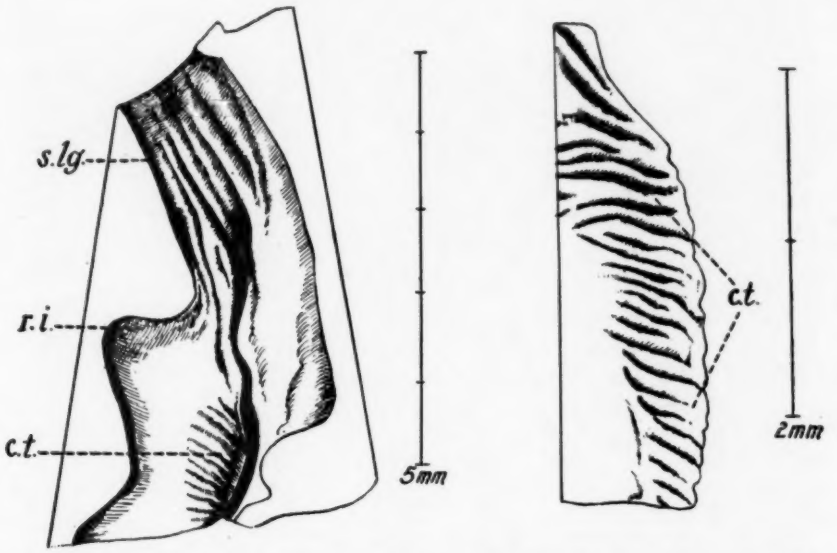

Fig. 7.—Drawing, after Turkewitsch [7] illustrating the aqueductal channel in the fetus and showing the folds over the colliculus tegmenti (*c.t.*); the other landmarks are the recessus isthmi (*r.i.*) and the sulcus longitudinalis (*s.lg.*).

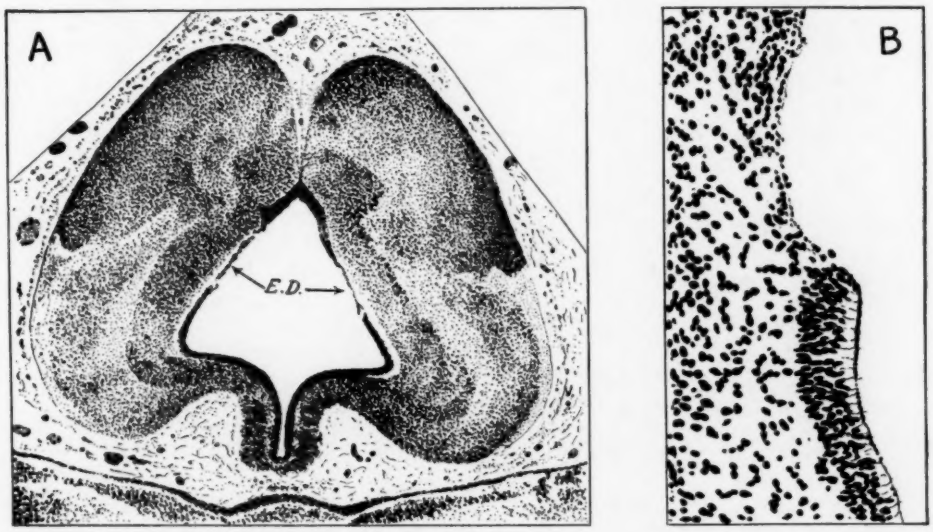

Fig. 8.—*A*, drawings, after Hochstetter,[8] illustrating the site in the midbrain sac in which the ependymal lining is missing (*E.D.*). *B*, the denuded area, shown in *A* (*E.D.*), under higher magnification.

ing from the embryonic elements in the basal plate of the aqueduct would tend to be directed in its growth into the aqueduct.

CASE 2.—*History.*—I. R., a man aged 56, entered the Mount Sinai Hospital on Aug. 24, 1928. He had been in good health until three months before admission, when he began to complain of intermittent headaches recurring nightly,

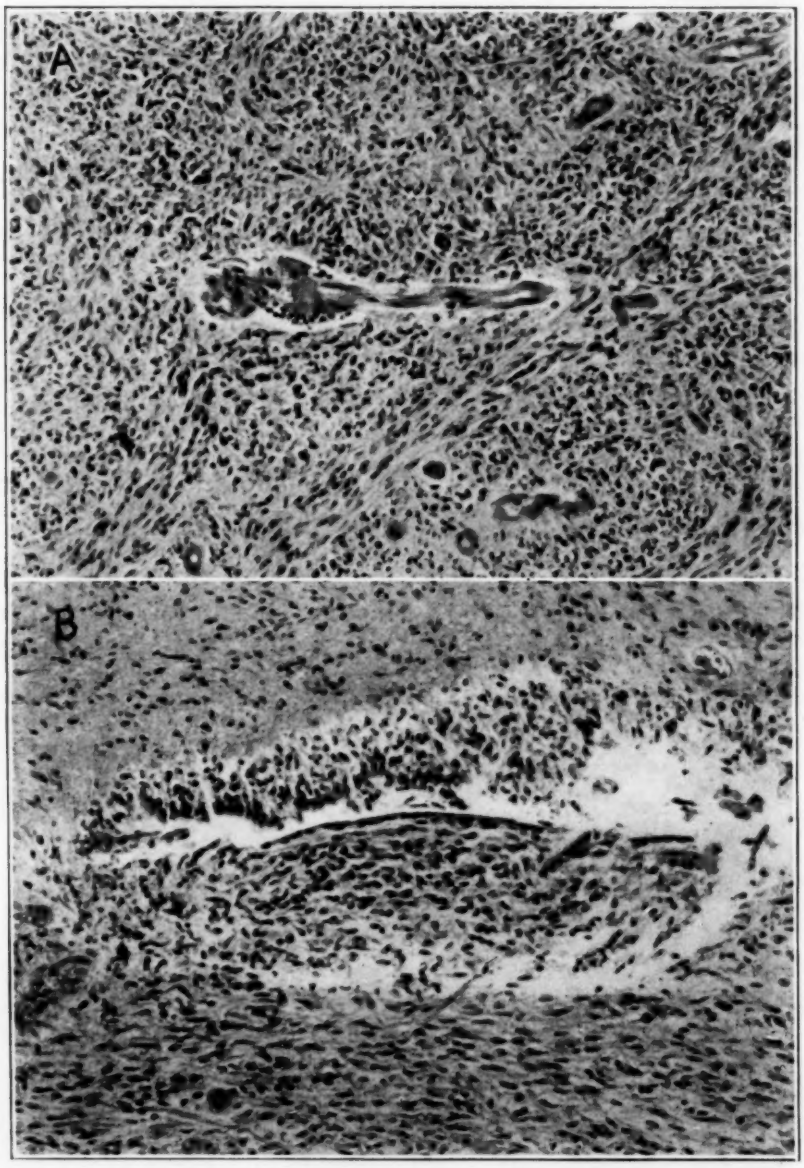

Fig. 9 (case 2).—*A*, section of tumor, showing the structure of a spongioblastoma multiforme. *B*, ependymal lining covering the tumor, with pseudostratified ependyma covering the normal tissue.

accompanied with dizziness, which persisted during the following day. His headaches gradually increased in severity and duration. Nine days prior to his admission it was noted that he was unable to turn his eyes to the left, and the

left side of his face became distorted and numb. Difficulty in swallowing appeared, and weakness developed in both lower extremities. A few days later he complained of double vision.

Examination.—The pupils were irregular and unequal, the left being larger than the right. Both pupils reacted poorly to light and in accommodation. The fundi showed extremely tortuous vessels, with slight blurring of the disk of the left eye. Both eyes were in conjugate deviation to the right. On his looking to the left, the right eyeball could be brought almost to the midposition, but the left eye remained deviated to the right. His voice was hoarse, and swallowing was difficult. There was a supranuclear paralysis of the left facial nerve. The pharyngeal reflex was greatly diminished. Hemiparesis with increased deep reflexes and a positive Babinski sign was present on the left side. Sensory examination showed diminished vibratory perception in the left lower extremity up to the iliac crest. Gait was ataxic, and there was a tendency to fall to the left. The blood pressure was 160 systolic and 110 diastolic. Lumbar puncture yielded clear cerebrospinal fluid. The Wassermann reactions of the blood and cerebrospinal fluid were negative, and the colloidal gold curve was normal.

Course of Illness.—There was rapid development of signs and symptoms. Paralysis of upward gaze, as well as lateral conjugate deviation of the eyes, appeared, with preservation of convergence. Speech became bulbar, and there developed paralysis of the left recurrent laryngeal nerve and hemihypalgesia and thermhypesthesia on the right side. Because of the rapid clinical course, a progressive intrapontile vascular thrombosis was suspected. His general condition became poor, and he died on Sept. 5, eleven days after admission.

Gross Necropsy Observations.—Section of the brain revealed a tumor, measuring about 3 cm. in diameter, in the midbrain. The growth involved the left cerebral peduncle in its entire length, extending dorsally into and displacing the tegmentum. The tumor extended caudally a short distance into the pons.

Microscopic Observations.—The tumor tissue was richly vascular and highly cellular. The cells contained deeply staining nuclei and were arranged in streams, whorls and rosettes, many without any definite pattern (fig. 9). The cell bodies were poorly defined. They were irregular in shape and stained poorly. Scattered among them were numerous giant cells, many of which were pyriform and contained several nuclei. The capillary walls were thickened, had a structureless, homogeneous appearance and were infiltrated with tumor cells. Within the tumor and the adjacent tissue were necrotic areas filled with debris and compound granular cells. These areas were surrounded by several layers of tumor cells in rosette formation. A segment of the tumor tissue was covered by normal ependyma. Pseudostratified ependymal epithelium covered the surface of a segment of normal tissue.

Comment.—Although the tumor in this case differed in its site of origin from that in the first case, both probably have embryonic residues as their source of origin. Two morphologic features, as Hochstetter emphasized in his observations on the midbrain, are responsible for the narrowing of the cavity of the embryonic midbrain, namely, the addition of fiber tracts and the proliferation and early migration of subependymal cells. Some of these cells become arrested in their migration, retain their embryonic proliferative potentialities and form centers of incompletely differentiated neuroectodermal elements. The source

of the second tumor is probably to be found in these heterotopic elements.

SUMMARY

Two cases of primary neuroectodermal tumors which had their primary site in the midbrain are described.

An attempt is made to correlate their source of origin with embryonic alterations in the developing midbrain.

Persistence of ependymal and subependymal cells, constituting a by-product of an excessive growth of ependymal folds which must undergo complete involution and obliteration, is considered the source of the tumor (transitional glioma) in the first case.

Persistence of migrated potent subependymal cells, forming centers of growth at a distance from the subependymal zone (heterotopias), suggests the origin of the tumor (spongioblastoma multiforme) in the second case.

The migration of subependymal cells represents an earlier phase in the development of the midbrain than the formation of subependymal folds. Therefore it is probable that the tumor arising from heterotopic elements is made up of less differentiated cell types than one arising from embryonic structures which make their appearance later in prenatal development.

TOXIC EFFECTS OF INTRATHECAL ADMINISTRATION OF PENICILLIN

A. EARL WALKER, M.D.
CHICAGO

PENICILLIN has been regarded as quite harmless even when administered in large doses and it is true that toxic manifestations are relatively rare as a result of parenteral administration. This is not the case when the drug is administered intrathecally, particularly if the dose is excessive. To illustrate this fact, which has not been generally recognized, two types of complications following intrathecal administration of penicillin are presented.

EXPERIMENTAL BASIS

In a series of experiments on the macaque monkey, on thirteen occasions 20,000 units of penicillin in 1 cc. of isotonic solution of sodium chloride was injected intrathecally. Within ten to fifteen minutes the animals were observed to look at, rub and then vigorously scratch their tails and perianal regions. This behavior persisted for at least an hour in some instances. In the monkey, these paresthesias appeared to be temporary, for the animal was well the following morning. The spinal cords of 5 macaque monkeys which had been given intrathecal injections of penicillin were examined. Although none of these monkeys showed clinical evidence of neural involvement at the time they were killed, 3 of the 5 spinal cords showed histologic alterations.

Sections from the lumbar portions of the spinal cord and the cauda equina were stained by Nissl's method, with hematoxylin and eosin with Perdrau's technic for reticulin and for myelin. In the cauda equina of 3 animals a patchy demyelination was present in the nerve roots. In these areas proliferation of the sheath cells was apparent. Between the roots of the cauda equina was a delicate proliferation of the arachnoid, binding together the roots of the cauda equina. Only an occasional lymphocyte was seen in the meshes of the arachnoid. The dura mater showed no alteration. The parenchyma of the spinal cord appeared relatively normal except for tigrolysis of an occasional anterior horn cell.

This work was carried out while Dr. Walker was assigned to the Cushing General Hospital, Framingham, Mass.

CLINICAL EVIDENCE OF TOXICITY OF THE DRUG

That similar radicular reactions may occur after the intrathecal injection of penicillin in man has previously been noted by a number of authors. Following the treatment of purulent meningitis by intrathecal injection of penicillin, Sweet, Dumoff-Stanley, Dowling and Lepper [1] noted that several of their patients exhibited disturbances of the bladder and paresthesias and weakness of the lower extremities. Walker and Johnson [2] reported a case of sacral radiculitis following the intrathecal administration of penicillin for a meningeal reaction secondary to a cholesteatoma of the mastoid. Their patient had urinary retention and severe motor and sensory disturbances in the legs. The dysuria cleared up rather quickly, but the other disturbances persisted for four months. As an illustration of this type of complication, the following case is presented.

REPORT OF CASES

CASE 1.—On Aug. 8, 1945, a soldier aged 32 fell from a second story window, sustaining a laceration over the right eye. The following day his temperature

TABLE 1 (case 1).—*Laboratory Findings and Results of Penicillin Therapy*

Date	Highest Temperature	Spinal Fluid: Cells per Cu. Mm.	Spinal Fluid: Polymorphonuclears, %	Spinal Fluid: Lymphocytes, %	Penicillin, Units: Intrathecally	Penicillin, Units: Intravenously	Comment
Aug. 10	40 C. (104 F.)	7,100	96	4	40,000	.....	Pneumococcus in cerebrospinal fluid
11	40	6,850	11	89	40,000	400,000	89% lymphocytes; culture sterile; voided
12	..	.....	..	..	20,000	380,000	800 cc. by catheterization; spinal tap unsuccessful
13	..	.....	..	..	.....	320,000	Spinal tap unsuccessful
14	..	1 cc. only 200	..	..	40,000	320,000	
15	..	.....	..	..	.....	320,000	
16	..	.....	..	..	.....	360,000	Patient catheterized
17	..	.....	..	..	.....	320,000	
18	..	.....	..	..	.....	320,000	
19	..	.....	..	..	.....	240,000	
20	..	20	..	..	.....	320,000	
Aug. 21 to Sept. 10						240,000	Sulfadiazine, 1 Gm./4 hr.
Sept. 10 to 21						120,000	Sulfadiazine, 1 Gm./8 hr.

was 100.4 F. A spinal puncture yielded a cloudy fluid, containing pneumococci on culture. The patient was given 40,000 units of penicillin intrathecally on the second, third and sixth days of his illness and 20,000 units intrathecally on the

1. Sweet, L. K.; Dumoff-Stanley, E.; Dowling, H. F., and Lepper, M. H.: The Treatment of Pneumococcic Meningitis with Penicillin, J. A. M. A. **127**:263-267 (Feb. 3) 1945.

2. Walker, A. E., and Johnson, H. C.: Principles and Practice of Penicillin Therapy in Diseases of the Nervous System, Ann. Surg. **122**:1125-1135, 1945; Penicillin in Neurology, Springfield, Ill., Charles C Thomas, Publisher, 1946.

fourth day (table 1). Shortly after the first intrathecal injection of penicillin he had difficulty in voiding and required catheterization. He recovered completely from the meningitis, but his urinary disturbances persisted. For five months after his meningitis the patient complained of pain about the left ankle and constipation. Examination revealed perianal hypesthesia and a severely atonic rectal sphincter. The knee jerks were equal and active. The ankle jerks were sluggish. Flexion of both knees and of the left foot was weak. The patient tired after walking one block. Examination of his spinal fluid four months after the meningitis revealed no abnormality.

The disturbances may be even more severe than those illustrated by case 1. An intense arachnoiditis associated with myelitis has been reported in a number of cases, and many more such instances have occurred which have not yet been recorded in the literature. Forrest [3] reported a case in which transitory pain and weakness developed in the upper extremities after the use of penicillin for meningococcic meningitis. Siegal [4] reported a case of transverse myelopathy following recovery from pneumococcic meningitis treated with penicillin intrathecally. Bailey [5] mentioned a case in which intrathecal administration of penicillin was followed by paraplegia and at a subsequent operation a marked leptomeningeal thickening was observed. It is true that Bailey ascribed the meningeal reaction not to the use of the drug but, rather, to the disease process. While it is impossible to state with certainty that the primary disease was not responsible for the complication, the fact that myelitis is a rare sequel of meningitis treated with sulfonamide drugs [6] and other agents [7] indicates that some other factor was responsible. After penicillin therapy for meningitis, especially if large amounts of the drug have been used, myelitis is not infrequent. A case is presented in detail to illustrate this complication.

CASE 2.—A married man aged 33 was admitted to Cushing General Hospital Dec. 17, 1945, because of paralysis of both legs, decubitus ulcers over the sacrum and hips and convulsive seizures. The patient was struck by shell fragments on Nov. 14, 1944, while digging a foxhole, sustaining wounds in the right frontoparietal region and the right supraclavicular region. He was not rendered unconscious and was able to walk to the field hospital, where his wounds were debrided. However, his left leg became weak, and on November 19 both the left arm and the left leg were paralyzed. The hemiplegia began to improve and two weeks

3. Forrest, A. R.: Neurological Complications in Cerebrospinal Meningitis Treated with Penicillin, Brit. M. J. **2**:805-806, 1945.

4. Siegal, S.: Transverse Myelopathy Following Recovery from Pneumococcic Meningitis Treated with Penicillin Intrathecally: Report of Case, with Note on Current Methods of Therapy, J. A. M. A. **129**:547-550 (Oct. 20) 1945.

5. Bailey, P.: Chronic Leptomeningeal Thickening Following Treatment of Meningitis with Sulfa Drugs, Ann. Surg. **222**:917-922, 1945.

6. Farmer, T. W.: Neurologic Complications During Meningococcic Meningitis Treated with Sulfonamide Drugs, Arch. Int. Med. **76**:201-209 (Oct.) 1945.

7. Degen, J. A.; Cameron, H.; Robinson, V. L. M., and Wieden, M. S. R.: Sequelae of Cerebrospinal Meningitis, Brit. M. J. **2**:243-247, 1945.

later was mild. On December 5 with procaine anesthesia, an abscess of the right frontoparietal region was evacuated, and fragments of bone were removed from the cavity. Because of cerebral herniation, a spinal puncture was performed and 25,000 units of penicillin instilled into the subarachnoid space. The cultures of the spinal fluid were sterile. Cultures of material from the wound yielded a nonhemolytic streptococcus. Approximately twelve hours later another spinal puncture was made. The fluid was said to be normal, but 15 cc. was removed and 50,000 units of penicillin in 10 cc. of isotonic solution of sodium chloride was instilled into the intrathecal space. The patient was also given 25,000 units of penicillin every four hours intramuscularly and 1 Gm. of sulfadiazine every four hours. On December 6 it was noted that both legs and the left arm were very weak and the patient was unable to void. A spinal puncture was performed, the initial pressure being 400 mm. of spinal fluid. After removal of fluid, 50,000 units of penicillin was injected intrathecally (table 2). On December 7 both legs were completely paralyzed. The next day, although the patient was mentally

TABLE 2 (case 2).—*Data on Clinical Course, Laboratory Study and Intrathecal Penicillin Therapy*

Date	Highest Temperature, C.	Spinal Fluid		Penicillin (Intrathecal), Units	Comment
		Cells	Cultures		
Nov. 14	.....	.....	.....	.....	Date of injury; primary débridement
19	.....	.....	.....	.....	Left hemiparesis
Dec. 2	.....	.....	.....	.....	Hemiparesis almost gone
5	.....	"Normal"	.....	25,000	Secondary débridement; drainage of abscess
6	37.8 (100 F.)	.....	Sterile	50,000	Unable to void; legs weak
7	38 (100.4 F.)	.....	Sterile	.....	Both legs paralyzed
8	38	.....	.....	.....	
9	.....	0	Sterile	.....	Left arm improving

clear, the paralysis of the legs remained unchanged. On December 14 the left arm could be moved but the legs remained paralyzed. No note was made regarding reflex or sensory disturbances until Jan. 5, 1945, when it was recorded that the reflexes of the lower extremities were absent and that there was sensory loss over the lower part of the body and legs.

On Jan. 22, 1945, the patient, on admission to O'Reilly General Hospital, had complete flaccid paraplegia, areflexia of the lower extremities and anesthesia below the level of the fourth thoracic dermatome. The tendon reflexes of the left upper extremity were more active than those on the right. On June 27, 1945, a tantalum cranioplasty was performed. Because of two convulsive attacks, the patient was transferred to Cushing General Hospital on Dec. 17, 1945.

At the time of his admission he was well nourished, but his skin was yellow from quinacrine (atabrine), although the scleras were clear. He had flaccid paralysis of both legs with absence of superficial and deep reflexes. The upper and middle abdominal reflexes were present on the right side. The abdominal reflexes were absent on the left side. The tendon reflexes of the left upper extremity were more active than those of the right, and there was a questionable Hoffmann sign in the left hand. Healed wounds were present in the right supraclavicular area and the right temporoparietal region of the scalp. No scar was present over the cervical portion of the spine. A urethral catheter was kept in place for tidal drainage of the bladder. The spleen was palpable approximately

3 cm. below the costal margin and the liver barely palpable. There was a large decubitus ulcer over the sacrococcygeal region, extending almost to the anus. The base was covered by fairly clean granulation tissue except for the upper part, which had a skin graft. Over each greater trochanter was an ulcer 3 cm. in diameter. On Jan. 30, 1946, the ulcers over the trochanters were closed by rotation flaps. The wound on the left side broke down because of formation of a hematoma, and a secondary closure was made on Feb. 15, 1946; and at the same time a split thickness graft was placed over the granulating sacral ulcer. The wounds healed well after this procedure. On March 21, 2 cc. of "pantopaque"

Photograph of the operative field in case 2, showing the considerable leptomeningeal thickening. The dura mater is held open by silk sutures.

(an iodized poppyseed oil, with special cohesive properties) was injected into the cisterna magna and observed under the fluoroscope to flow freely to approximately the third cervical vertebra, where it seemed to stop. With lumbar puncture, 2 cc. of "pantopaque" was injected into the subarachnoid space at the fourth lumbar vertebra. Fluoroscopically, the medium was observed to flow to the interspace between the eighth and the ninth dorsal vertebra. It was then seen that the small amounts of the medium injected into the cervical region had reached the seventh cervical segment. The contrast medium was collected in small globules on either side of the spinal cord. Roentgenograms taken one week later showed

small drops of "pantopaque" scattered throughout the dorsal portion of the spinal canal with larger collections of the medium overlying the interspace between the twelfth dorsal and the first lumbar vertebra and that between the third and the fourth lumbar vertebra. There was a rather uniform distribution of the droplets throughout the dorsal region. Roentgenograms of the skull showed no evidence of the contrast medium in the intracranial cavity. It was thought that arachnoiditis would best explain the roentgenographic findings.

On March 27, 1946, with the use of procaine anesthesia, a laminectomy was performed. Along the site of the proposed incision in the mithoracic region, 1 per cent procaine hydrochloride was injected. The spinous processes from the fourth to the seventh thoracic vertebrae inclusive were then removed and their laminas rongeured away. The dura mater was then opened. It was observed to be strongly adherent to the underlying pia-arachnoid, and only with great difficulty were the two separated. The arachnoid was then seen to be 2 to 3 mm. thick, and it was difficult to detect the division between the arachnoid and the spinal cord. Near the upper third of the exposed area, a cyst, 1 cm. in length and 5 mm. in width, was observed, covered by greatly thickened arachnoid. On opening it, a small amount of spinal fluid was seen to pulsate with respiratory and cardiac activity. About this cyst was thickened arachnoid, and on its medial surface was what appeared to be a greatly sclerosed spinal cord (figure). A small piece of arachnoid was taken for biopsy. The dura mater was then closed, with strips of fibrin foam laid over the line of suture. The muscles were then approximated and the edges of the skin brought together with silk sutures. The patient had an uneventful convalescence from this procedure, and the wound healed by primary intention. His neurologic status remained unchanged.

Examination of the tissue removed at operation was reported by Capt. J. Churg as showing dense fibrous tissue in parallel layers with numerous small fibrocytic nuclei. Embedded in the tissue were small bundles of nerve fibers showing moderate edema and some degenerative changes. Occasional collections of small round cells were present.

COMMENT

It is known that intrathecal medication may produce leptomeningeal reactions, and many substances when injected into the subarachnoid space have been found to be responsible for such alterations in the arachnoid. That penicillin may give rise to the same result is not unexpected. Whether the primary effect of the drug is on the leptomeninx or the nerve tissue cannot be determined from this study. In view of the rapid onset of the reaction in some cases, it would seem probable that the nerve tissue was damaged early. On the other hand, the arachnoidal alterations appeared to precede the neural damage in the experimental neuropathy induced in monkeys by intrathecal injection of penicillin.

In the cases presented, and in most cases of similar complications reported in the literature, the amount of penicillin administered at one time was greater than is usually advised. Whether the concentration of the penicillin or the total amount given is the more potent factor in producing this complication is difficult to determine, for usually a large dose is associated with a high concentration of the drug. It would seem,

however, that intrathecal administration of penicillin in doses not in excess of 20,000 units and well diluted with the spinal fluid is unlikely to cause this complication.

There is no evidence that the use of very large amounts of penicillin is more effective in the treatment of purulent meningitis than the use of moderate doses, provided the penicillin is thoroughly distributed throughout the subarachnoid space. An adequate antibiotic level throughout the entire subarachnoid space can be obtained with the use of penicillin given into the cisterna magna or into the ventricle, thus eliminating the necessity of large doses in the lumbar region. Experimental studies on both animal and man have shown that the distribution of penicillin when so given is superior to that when the drug is administered in the lumbar region.

SUMMARY

Two cases illustrating types of neural reaction to intrathecal administration of penicillin—radiculitis and myelopathy associated with chronic leptomeningeal thickening—are presented. Such reactions usually occur only when large amounts of penicillin are injected into the subarachnoid space. When moderate or small doses of the drug are used, the complication is rarely encountered.

950 East Fifty-Ninth Street, Chicago (37).

DYSTONIC FORM OF AMAUROTIC FAMILY IDIOCY

Report of a Case

ALUIZIO MARQUES, M.D.
RIO DE JANEIRO, BRAZIL

AMAUROTIC family idiocy has rarely been described in Brazilian literature. The infantile form of the disease was studied and described by Julião, Magalhães and Brandi. Marques [1] (1943) reviewed the subject and presented a case characterized by amaurosis, atrophy of the optic nerve, pigmentary retinosis, muscular hypotonia, convulsions, mental regression and the added stigma of spina bifida. The purpose of this paper is to present a case of amaurotic family idiocy in which diagnosis was possible only after careful histologic study.

REPORT OF CASE

The patient was first seen in the neurologic clinic of the Getulio Vargas Hospital at the age of 17 years. After preliminary examination, he was admitted to the hospital, with well defined signs of a dystonic syndrome, characterized by slow and spasmodic twitching of the face, spasmodic twitching of the trunk and neck and slow and spasmodic hyperkinetic movements of both the upper and the lower extremities.

The family history revealed that the patient's mother and father were living and well and were not blood relatives. The family antecedents were Brazilians of Portuguese extraction, not of Jewish origin. There was no history suggestive of neurologic disease in any member of the family except for 1 sibling, aged 9, who for the past two years had had neurologic signs similar to those presented by the patient.

The birth of the patient had been normal, no forceps being used. The weight at birth was 7 pounds 8 ounces (3,400 Gm.). He had had no serious disease or operation. He was said to have grown and developed well up to 9 years of age. At the time of examination he was 4 feet 11 inches (149 cm.) in height and weighed 106 pounds (48.1 Kg.). There were no bodily deformities; the face presented twitchings. Examination of the heart, lungs and abdomen revealed nothing abnormal. The pulse rate was 80 and the blood pressure 110 systolic and 60 diastolic. The blood and the cerebrospinal fluid gave negative reactions for syphilis.

The parents dated the onset of the illness to the age of 9 years. Prior to that time the child had been entirely normal, physically and mentally, and he was progressing well in school. At the age of 9, dysarthria and a mild intention tremor developed, and progressive mental deterioration was noted. No visual disturbances

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From the Neurological Clinic of the Getulio Vargas Hospital.

1. Marques, A.: Idiotia amaurótica familiar: Estudo de um caso pessoal e revisão da casuística brasileira, Arq. neuro-psiquiat., São Paulo **1**:207-233 (Dec.) 1943.

occurred. Gradually progressive, slight dystonia was noted through the years by the parents, whose story may be regarded as only fairly reliable. This dystonia eventually progressed to hypertonia and hyperkinesis, and profound dementia developed.

Physical examination revealed a well developed, well nourished white youth. The outstanding features on inspection were a slow, spasmodic twitching of the face, trunk and neck; hyperkinesia of the upper and lower extremities, and extreme voluntary hypermotility (fig. 1 *A*). Gross inspection revealed abnormally large feet, with the characteristic hollowing observed in status dysraphicus (fig. 2).

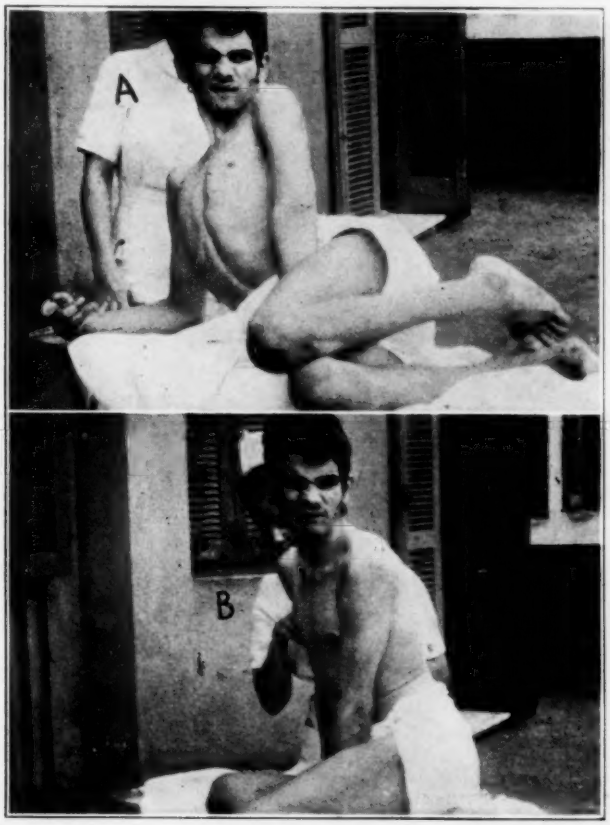

Fig. 1.—Cinematographic reproductions of a patient 17 years of age, showing (*A*) athetosis of the lower extremities and tonic distortion of the trunk and neck and (*B*) movements of the face.

The patient presented no ocular disturbances, nor was there paralysis of the muscles of the eyeball, either external or internal. The photomotor reflex was normal. Examination of the fundus showed that the retina, optic disk, veins and arteries were normal.

The clinical impression was that of hepatolenticular degeneration (Wilson's disease) or Hallervorden-Spatz disease.

The patient died four months after entering the hospital. The clinical picture remained unchanged from the date of admission, but, as he ate little and had diarrhea, he suffered gradual starvation and marasmus and finally died in a state of cachexia.

Histologic examination of the retina showed nothing abnormal. The optic disk and the optic nerve were normal.

Macroscopic and microscopic examination of the viscera (heart, lungs, liver, spleen, kidneys and digestive organs) revealed nothing significant except for slight atrophy of the heart muscle and slight signs of degeneration of the liver, changes

Fig. 2.—Hollow plantar arch and distorted toes, produced by the athetosis constantly shown by a patient with amaurotic family idiocy, dystonic form.

which might be attributed to the state of cachexia that preceded death. In the intestine, especially the colon, there were signs of inflammation, referable to the enteritis which manifested itself during the latter part of the patient's life.

Histologic study of the liver and brain ruled out a consideration of hepatolenticular degeneration. Further histologic study (W. E. Mafei) led to the belief that the patient presented a form of amaurotic family idiocy without ocular involvement.

Histologic examination revealed marked alteration of the nerve cells, including those of the cerebral cortex, basal ganglia, thalamus, cerebellum, pons, medulla and spinal cord. Only minor variations were noted in the intensity of the process in the different regions. The Nissl stain revealed that the cells were enlarged and balloon shaped, with the nucleus displaced to the periphery (fig. 3). The cytoplasm was delicate in appearance, but was occasionally spongy, containing large vacuoles. The chromophilic substance was dense and stained deeply near the nucleus but was otherwise sparse and did not take the stain well. The nuclei in general, except for their peripheral position, had a rather normal appearance and were only occasionally hyperchromic.

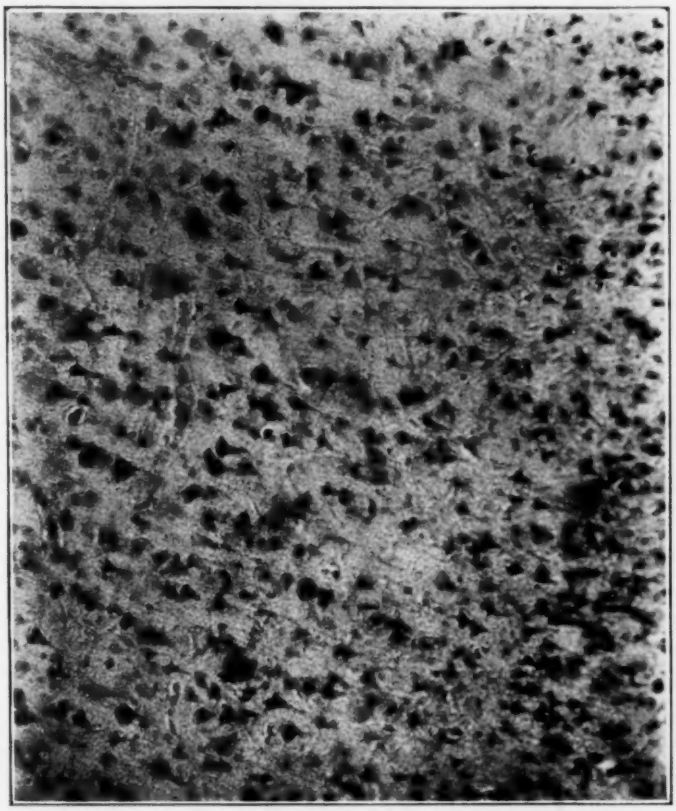

Fig. 3.—Section of the cerebral cortex of the frontal lobe of a patient with amaurotic family idiocy, showing the balloon-shaped cells. Nissl method; Leitz ocular 4; objective 5.

The Weil stain for myelin, as well as the Bielschowsky method, revealed nothing of interest in the white matter of the brain, nor were the neurofibrils abnormal. As previously mentioned, the outstanding characteristic was the wide distribution of the balloon-shaped cells, which gave very similar pathologic pictures in the cerebral cortex, the basal ganglia (fig. 4) and the substantia nigra.

The swollen area of the nerve cell contained granules which stained deep red with sudan III, suggestive of prelipid granulation and lipofuchsin. Around capillaries in the cerebral cortex and the basal ganglia the same pigment was seen. In addition, the capillaries showed calcification.

In sections stained with Weil's myelin technic, the predominance of the fibers in the globus pallidus presented a picture of status fibrosus. The Globus method for macroglia showed hyperplasia of the pyramidal cells in the third layer of the prefrontal area of the cerebral cortex (fig. 5). The balloon-shaped cells, with loose, delicate cytoplasm and peripheral nuclei (figs. 6 to 10), together with the changes revealed with special stains and the distribution of the pathologic factors pointed to a diagnosis of amaurotic family idiocy.

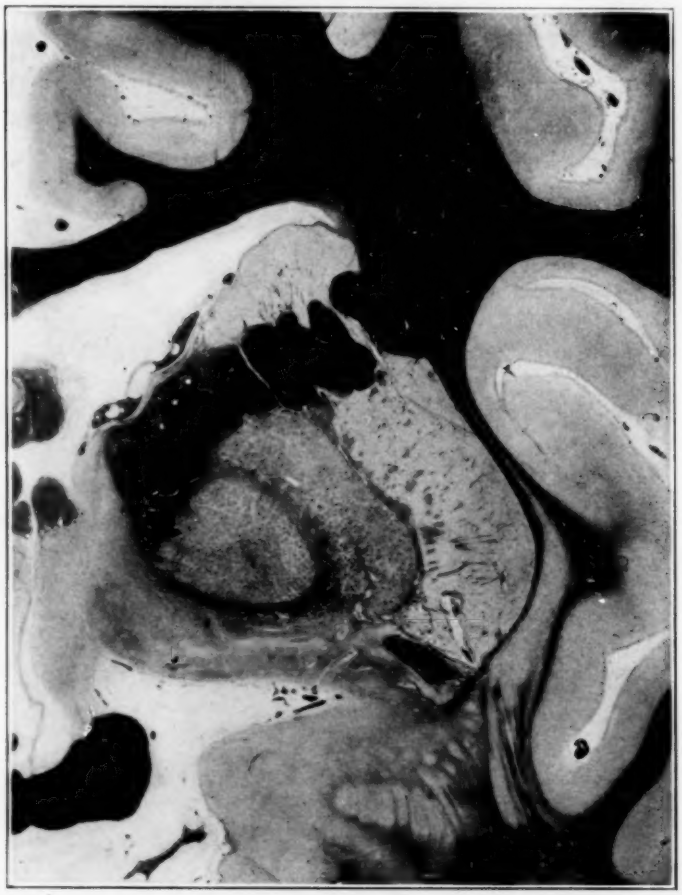

Fig. 4.—Section of the corpus striatum, showing the abundance of fibers. Weil method for myelin; Leitz microsumar lens, 8 mm.

COMMENT

A review of the literature on amaurotic family idiocy, including publications by Globus,[2] Hassin, Vogt, Spielmeyer,[3] Josephy,[4] Sjögren

2. Globus, J. H.: Amaurotic Family Idiocy, J. Mt. Sinai Hosp. **9**:451-503 (Nov.-Dec.) 1942.

3. Spielmeyer, H. W.: Zur Pathogenese örtlich elektiver Gehirnveränderungen, Deutsche Ztschr. f. Nervenh. **89**:13-17, 1926.

4. Josephy, H.: Familiäre amaurotischen Idiotie, in Bumke, O., and Foerster, O.: Handbuch der Neurologie, Berlin, Julius Springer, 1936.

and Sjövall, revealed no case in which the picture was similar to that in the one described here. The literature shows no case of amaurotic family idiocy presenting the extrapyramidal syndrome described in this case. The hypokinetic and akinetic symptom complex described by Sjögren and Sjövall, while having a possible extra pyramidal origin, in no way resembles the dystonic form described in this case.

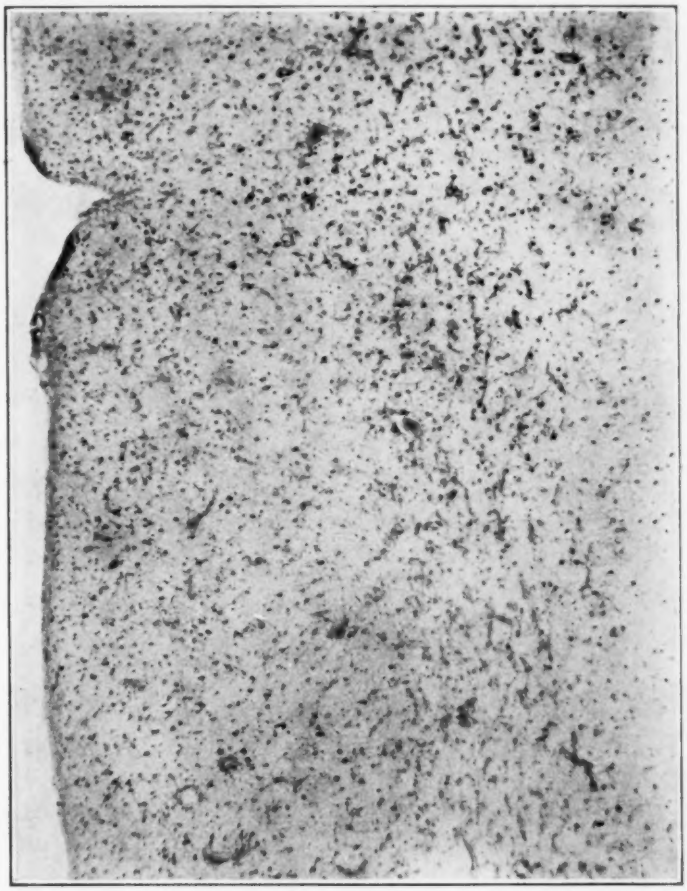

Fig. 5.—Hyperplasia of the astroglia in the third layer of the cerebral cortex of the frontal lobe. Globus method; Leitz ocular 4; objective 3.

Amaurotic family idiocy (Tay-Sachs disease) is distinct from the juvenile form (Spielmeyer-Vogt disease). The juvenile form is characterized by dementia acquired between the ages of 8 and 14 years and by epilepsy, atrophy of the optic nerve and, finally, blindness; often modification of the retinal pigment occurs. The clinical picture that has been described for the juvenile form does not adequately cover all the verified cases of the disease. Though Spielmeyer considered the

clinical diagnosis to be extremely difficult, Sjögren and Sjövall presented what they considered classic pictures and claimed that there were only slight variations in individual cases. According to the latter authors, the child develops normally up to the age of 5 to 8 years. At some time during this period disturbance of vision occurs and symptoms of mental regression are noted. Epileptiform attacks begin and increase, in both frequency and severity. The symptoms referable to the extra-

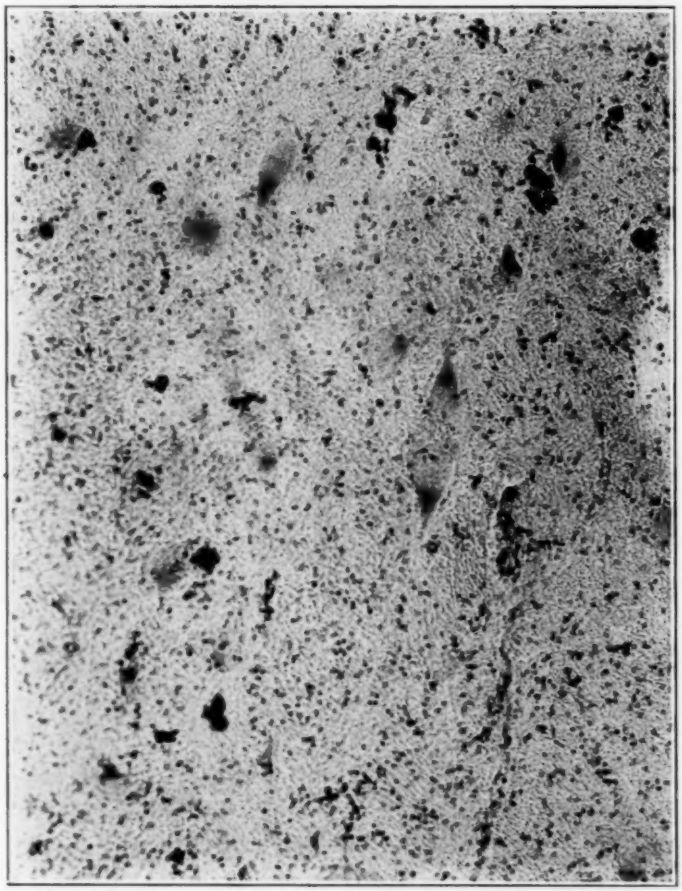

Fig. 6.—Section of the corpus striatum, showing lightly stained, balloon-shaped cells. Nissl method; Leitz ocular 4; objective 5.

pyramidal system then develop; they were said by Sjögren and Sjövall to be the most prominent feature of this form of the disease. The extrapyramidal involvement results in a constantly increasing rigidity of body posture, loss of associated and automatic movements, retardation and, finally, absence of voluntary movements. If voluntary movement is not completely lost, a disturbance in gait, characterized by short steps, occurs. This is followed by disturbances in equilibrium. As the dis-

ease progresses, paraplegic atrophy of the lower extremities begins; apathy deepens, and then all voluntary movement ceases and the marasmic patient dies of intercurrent disease, usually about the seventeenth year of life.

Pathologically, amaurotic juvenile idiocy can be classified with forms of neuroganglionic degeneration, involving all parts of the neuraxis and varying widely in extent, according to the region affected. It

Fig. 7.—Section of the corpus striatum. No hyperplasia of the glia is to be seen. The cells present a balloon-shaped aspect. Globus method; Leitz ocular 4; objective 5.

is these regional variations that probably explain the well defined and diverse clinical types described by various authors.

The pathologic picture shows the characteristic feature that Schaffer [5] stated to be fundamental in hereditary diseases of the nervous system,

5. Schaffer, C.: Pathogenesis of Amaurotic Idiocy, Arch. Neurol. & Psychiat. **24**:765-774 (Oct.) 1930; Zur Pathogenesis der Tay-Sachs'schen amaurotischen Idiotie, Neurol. Centralbl. **24**:386-437, 1905; General Significance of Tay-Sachs Disease, Arch. Neurol. & Psychiat. **14**:731-741 (Dec.) 1925.

namely, ganglionic selectivity of the pathologic process, the mesodermic elements being completely spared. The pathologic process affects only the tissues derived from the neurectoderm. The condition may therefore be termed a selective germ layer disease. Schaffer stated that the disease involves principally the hyaloplasm of the affected cells; in the cytoplasm without basic structure swelling occurs first. After this,

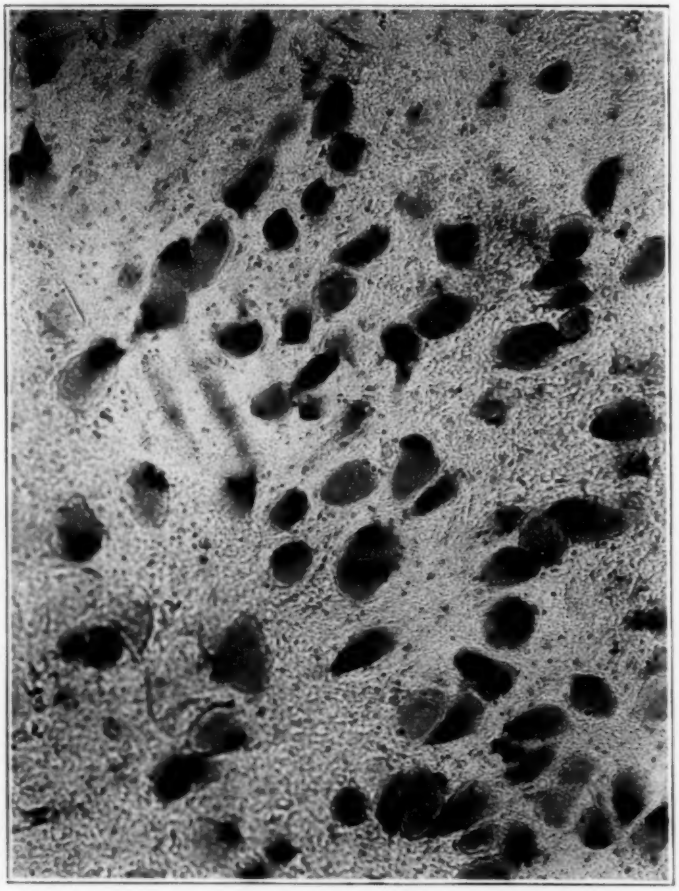

Fig. 8.—Section of the substantia nigra. Balloon-shaped cells are evident; the interstitial tissue appears rarefied and granulated. Nissl method; Leitz ocular 4; objective 5.

a granular material appears, which fills the cytoplasmic area. Schaffer called this material prelipid granules; as distintegration proceeds, these granules are converted into simpler fatty substances. According to Schaffer, the final alteration in this disintegrative process takes place in the body of the glia cells, and these cells act as macrophages. Strauss and Sachs published material that has confirmed both Schaffer's obser-

vations. Recently, further pathologic work on other forms of the disease affecting the cerebellum and the white matter of the brain has been carried out, notably by Globus and Hassin.

The pathologic process in amaurotic family idiocy appears to be ubiquitous and shows a preferential distribution, which distribution is reflected in the clinical picture. The change in the metabolism of the cytoplasm, which centers in the prelipid granules, seems to constitute the

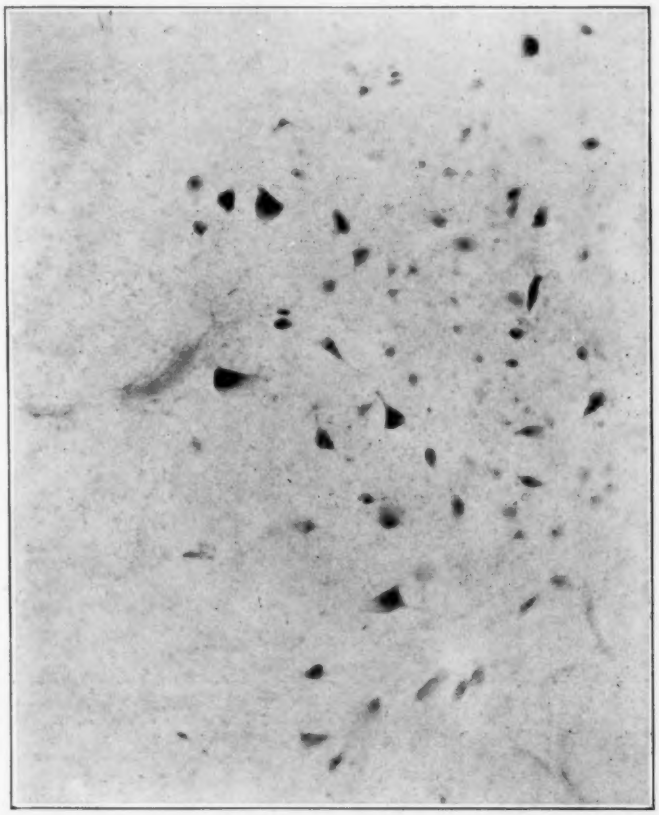

Fig. 9.—Histologic section of the medulla. Balloon-shaped appearance of the cells of the hypoglossal nucleus. Nissl method; Leitz ocular 4; objective 3.

foundation of the pathologic process. This occurs in infancy and progresses, leading always to death. There seems to be a definite relationship between senile involution and amaurotic family idiocy, an analogy which has been noted by Marinescu.

The sudanophilic lipids which are observed in the juvenile form and in other types of amaurotic family idiocy present a picture identical with the pigments observed in senile involution, in the cells of patients dying in the fifth, sixth and seventh decade of life.

SUMMARY

A brief review of amaurotic family idiocy is given, and a case is reported, with results of pathologic examination. The outstanding clinical feature of the case presented was a type of dystonia identical with that observed in Wilson's disease and in the Hallervorden-Spatz syndrome. There was mental deterioration, but no amaurosis or other ophthalmic change.

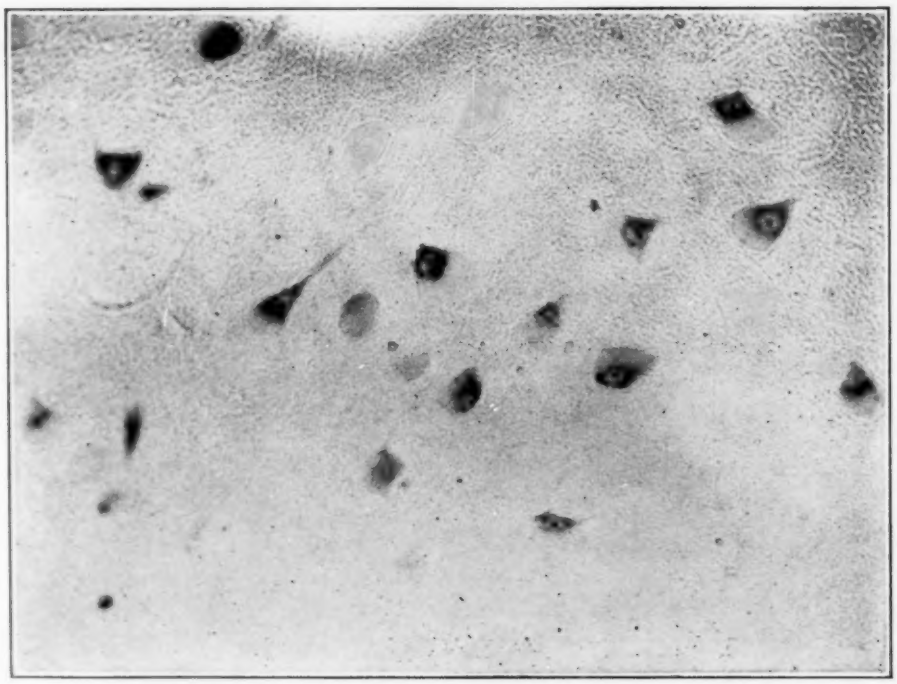

Fig. 10.—Balloon-shaped cells in the anterior horn of the spinal cord. Nissl method; Leitz ocular 4; objective 5.

The diagnosis of amaurotic family idiocy was made possible by histopathologic study, which revealed a pronounced change in the nerve cells in all nerve tissues examined, including the cerebral cortex, corpus striatum, pons, medulla and spinal cord.

It is believed that this process is a heretofore undescribed form of the disease, which might properly be called a dystonic form of amaurotic family idiocy.

Marques de são Vicente 316.

CONGENITAL CYST OF THE SPINAL MENINGES AS CAUSE OF INTERMITTENT COMPRESSION OF THE SPINAL CORD *

RAYMOND D. ADAMS, M.D.
AND
WALTER WEGNER, M.D.
BOSTON

IN RECENT years we have had occasion to observe and study 2 unusual cases in which the spinal cord was intermittently compressed by a solitary cyst in the meninges. The cysts were filled with a mucinous material, were lined with ciliated epithelium and had a wall composed of fibrous connective tissue, bone and cartilage. They were situated in the spinal subarachnoid space, and the one of which the anatomic relationships could be ascertained was connected by a narrow stalk of connective tissue to the dura. Because of their morphologic characteristics, we are inclined to believe that these meningeal cysts are quite different from the usual dermoid, meningocele or meningomyelocele. Although similar cases have been reported, we ourselves were not hitherto familiar with this condition and believe that the average neurologist is not acquainted with it. The purpose of the present communication is to set these 2 cases on record and to discuss the nature and pathogenesis of this cyst.

REPORT OF CASES

CASE 1.—*History.*—An Italian casket maker aged 41 entered the Boston City Hospital on Sept. 26, 1941, because of pain in the lower part of the back and the buttocks and weakness of the legs. The present illness began in 1928, when for the first time he had a pain in the lumbar region. It came on gradually without antecedent injury and became steadily more intense until he was unable to work. He was admitted to a hospital and a plaster spica was applied, but during the next twenty-five days he obtained no relief from the pain. A tonsillectomy was

From the Neurological and Neurosurgical Service, Boston City Hospital, and the Departments of Neurology and Surgery, Harvard Medical School.

* Dr. Herbert Block, of the Department of the Classics, Harvard College, suggested that this condition be called meningocystitis spinalis congenita. The first word is newly formed and is latinized Greek, and the last two words are Latin adjectives already in common use. Latinized Greek terms are objectionable to purists in language, but their use is customary in medical science. The word "teratomatous," which has been used by other authors to designate this cyst, is pseudo-Greek; its only genuine element is τέρας, meaning "monster," and does not imply the congenital nature of the cyst.

then performed, and later "electric treatment" and hydrotherapy were given, without effect. During this illness the right leg was noted to be weak. These symptoms then all subsided spontaneously.

During the next four years the patient remained well, and then, in 1932, the pain recurred in the same region of the back. This time he was in the hospital for seven weeks. Adhesive strapping and local application of heat were used, and the pain disappeared.

In 1935 the patient went to the hospital after having had severe pain in the lumbar region for about ten weeks. The findings on physical examination were said to have been normal, and roentgenograms of the spine and pelvis revealed no abnormalities. After being in the hospital five days, he was discharged as improved. One year later he had an operation for an undescended left testis and inguinal hernia. While he was convalescing, pain in the back recurred, and a plaster spica was applied for six weeks, without benefit. Again, the pain disappeared after a few weeks.

The patient remained well and worked regularly until the summer of 1941, at which time the pain in the back returned. This time it was accompanied with weakness and numbness of the legs. Urgency and precipitancy of urination also developed. He recalled that on one occasion his legs gave way and he collapsed to the floor. At the time of admission to the hospital the pain in the back had extended to the right side of the chest and across the upper abdominal quadrant on the right side.

Examination.—The patient was well developed and appeared healthy. He was oriented and rational and gave an adequate history. The only abnormal physical signs were those referable to the nervous system. The cranial nerves and upper extremities functioned normally. There was moderate weakness of all the muscles of both legs, more pronounced on the right than on the left. The muscles of the right leg were slightly atrophied, especially the quadriceps group, where fascicular twitches were seen. The muscular tone was approximately normal. The abdominal muscles were also weakened, so that the patient was unable to sit up except with the aid of his arms. The knee jerk was absent and the ankle jerk hyperactive (3 plus) on the right side; both reflexes were 2 plus on the left side. The abdominal reflexes were absent, and the plantar reflexes were equivocal, probably extensor in type. On the right side of the body there was pronounced reduction in pain and temperature sensations from the sixth thoracic to the first sacral segment, and from the first sacral to the fifth sacral these sensations were slightly impaired. On the left side pain and temperature sensations were impaired from the first lumbar to the fifth sacral segment. Touch sensation was normal throughout these areas. Vibratory and postural sensations were diminished below the hips. There was tenderness on percussion of the spines of the lower thoracic and lumbar vertebrae.

Laboratory Data.—The blood count and urinalysis gave values within normal limits. The cerebrospinal fluid was under a pressure of 180 mm., was slightly yellow and contained 4 lymphocytes per cubic millimeter and 154 mg. of protein per hundred cubic centimeters. There was a partial dynamic block, as evidenced by the slow fall of pressure after jugular compression. The serologic reactions of the blood and the Wassermann and Davies-Hinton reactions of the spinal fluid were all negative. With injection of 5 cc. of iodized poppyseed oil into the lumbar sac, it was possible to demonstrate a block at the twelfth dorsal vertebra.

Course.—A laminectomy was performed on October 3. There was thinning of the laminas of the eleventh and twelfth thoracic and first lumbar vertebrae,

and the epidural space was reduced. The dura was thin and seemed distended. Beneath the dura was a whitish tumor, which was lightly adherent to both the dura and the arachnoid in some areas. It extended from the lower border of the tenth thoracic to the second lumbar vertebra. This tumor appeared to merge with the cord laterally and could not be dissected free. When incised, it was observed to consist of a thin-walled cyst filled with a whitish mucoid material. When the contents were removed by suction, there was nothing left but a thin, parchment-like shell of the cyst wall. The spinal cord was severely compressed by this cyst. No communication between the central portion of the spinal cord and the cyst could be demonstrated. A catheter was inserted upward and downward in the subdural space without encountering any obstruction.

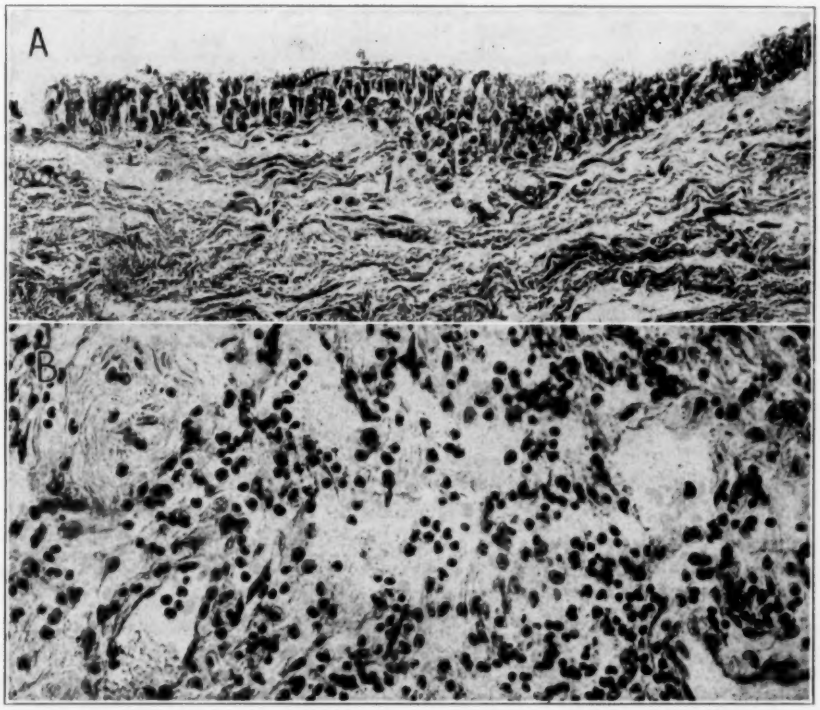

Fig. 1.—*A*, photomicrograph of wall of the cyst, showing fibrous connective tissue and ciliated columnar epithelium; phosphotungstic acid hematoxylin stain. *B*, focus of polymorphonuclear leukocytes, lymphocytes, plasma cells and histiocytes in the wall of the cyst.

The postoperative course was satisfactory, and at the time of the patient's discharge, on October 28, he was free of pain, showed no sensory impairment and was able to walk easily. At this time his bladder did not empty completely; there was a residuum of 150 cc. at the end of urination. Reexamination on December 10 showed that the patient still had slight weakness and flabbiness of the muscles of the right leg. The right ankle jerk was now diminished. He still experienced a mild pain around the lower right part of the thorax, and there was mild hypalgesia from the ninth thoracic to the first lumbar dermatome on the right side. He returned to his job at this time. When last seen on April 7, 1942, he had no complaints except for mild weakness in the right leg.

Pathologic Observations.—Several small pieces of the wall of the cyst were submitted for histologic examination. The wall was composed of collagenous connective tissue, in which there were numerous small arteries and veins and, in one place, a fascicle of nerve fibers. The cyst was lined with ciliated epithelium (fig. 1 *A*); the lining had a thickness of several cell layers. In places the connective tissue was infiltrated with polymorphonuclear leukocytes and macrophages. Fibroblasts were actively proliferating in these regions (fig. 1 *B*). Focal collections of lymphocytes and plasma cells were also present. There was no glial tissue in the wall. The pathologic diagnosis was teratomatous cyst of the spinal meninges.

Case 2.—*History.*—A man aged 29 was admitted to the hospital on Dec. 6, 1945, because of paralysis of his arms and legs and difficulty in breathing. In the past six years he had had at least five episodes similar to the one which led to his latest admission to the hospital.

In July 1939 he first began to have a rather severe pain in his neck. About the time of onset of the pain he had fallen downstairs, but the accident did not seem to bear a causal relationship to his symptoms. Then, over a period of a few days, his right arm and both legs became paralyzed. On the day of his admission to the hospital his left arm also became paralyzed. Examination at this time disclosed a patient who was drowsy and confused. There were no abnormalities of the cranial nerves. The right arm and leg were completely paralyzed, and the left limbs were so weak that only a few feeble movements were possible. The paralyzed muscles were of normal bulk and were flaccid. All the tendon reflexes were obtainable, though sluggish; the plantar reflex was equivocal on the right and absent on the left. No definite sensory changes could be detected. The cerebrospinal fluid was under a pressure of 250 mm. of water; the fluid was slightly yellow; it contained no cells, but the total protein was 249 mg. per hundred cubic centimeters. The patient was placed in a respirator, and no further progression of neurologic symptoms occurred. He began to improve during the fourth week in the hospital. Subsequent lumbar punctures on August 24 and September 8 revealed total protein values of 59 and 25 mg. per hundred cubic centimeters, respectively, and the dynamic pressure was said to be normal on both occasions. At the time of discharge the patient still showed great weakness of his limbs, more pronounced on the right side, but was able to walk with assistance. He returned to his home, and within a few weeks he had recovered normal control of his limbs. The only residual symptom was a slight dragging of the right leg when fatigued. The only two clinical diagnoses which were seriously considered were acute infectious polyneuritis and acute multiple sclerosis.

One year later the patient had recurrence of the pain in his neck and weakness of the right arm, which lasted one week. In June 1943 he began to experience a burning pain in the right side of his neck and within a few days had almost complete paralysis of all four extremities. The order of paralysis was again the right arm, right leg, left leg, trunk and left arm. There were no paresthesias in the right hand. Examination at this time (June 15) showed an alert, well oriented man, whose neck was rather stiff. The right pupil was smaller than the left, and sweating was reduced over the right side of the face. All extremities were completely paralyzed. There were slight atrophy and some spasticity of the right arm and leg. Tendon reflexes on the right side were 3 plus, whereas those on the left side was 2 plus. The right plantar reflex was extensor and the left one flexor. The patient was incontinent of urine and feces. There was impairment of all forms of sensation below the fourth cervical segment. The dynamic pressure of the spinal fluid was said to have been normal, and the total protein content was 364 mg. per hundred cubic centimeters; there were no cells, and the Wassermann reaction was negative. On June 23 the total protein was

444 mg.; on June 28 it was 375 mg. and on July 15 it had fallen to 25 mg., per hundred cubic centimeters. Thrombophlebitis developed in the left leg in the early part of July, and on July 9 bilateral ligation of the saphenous vein was done. The paralysis became more pronounced until it was impossible for the patient to make a single movement of any part of his body. By September 11, however, considerable improvement was noted, and this continued, so that by November 6 he was able to walk if assisted by two persons. At this time the tendon reflexes were still hyperactive on the right side and the plantar reflexes were extensor bilaterally. Sensory impairment was less severe, being now greatest in the left leg. At the time of his discharge, on December 18, there were still weakness of all four extremities and slight atrophy of muscles in the right leg. A tentative diagnosis of multiple sclerosis was made at the time of discharge. At home the improvement continued, and within two or three months the patient had completely recovered except for easy fatigability of the right leg.

In April 1944 the patient had an infection of the upper respiratory tract, which was followed by weakness of all four extremities. He remained at home in bed for three weeks with partial paralysis of his limbs and some urinary incontinence, but after a short time was able to get about once again. In September 1945 there was another episode of weakness of the right arm and both legs, which lasted about two or three weeks.

In November 1945 the patient again had an infection of the upper respiratory tract, and afterward his right leg dragged more than usual. He had pain in the right side of his neck. He became extremely constipated and had to resort to enemas. During the next two weeks the fingers of the right hand became numb and paralyzed, and in another three days both legs and the left arm became weak and numb. The patient was by this time incontinent. Spontaneous flexor spasms of the right arm and leg occurred intermittently. He was brought to the hospital because of respiratory difficulty, which had developed a few hours before admission.

Examination.—The temperature, pulse and blood pressure were normal. Respirations were shallow and depended entirely on movements of the diaphragm; the intercostal muscles were paralyzed. The patient was frightened and slightly confused. Shrugging of the shoulders was the only movement of the trunk or limbs of which he was capable. The legs were slightly spastic and in a position of extension. All the tendon reflexes were of about 3 plus activity and were brisker on the right side than on the left. The abdominal reflexes were absent; the right plantar reflex was extensor, while the left one was flexor. All forms of cutaneous sensation were absent on the right side below the fourth cervical dermatome and were impaired in a similar area on the left side. Vibratory sensation was partially retained in the hands and over the upper thoracic portion of the spine but was absent below this point. Postural sense was absent in the lower extremities and reduced in the hands and arms.

Laboratory Data.—The blood count and urinalysis revealed no significant abnormalities. The initial pressure of the cerebrospinal fluid was 205 mm. and the dynamic pressure was normal; the total protein was 78 mg. per hundred cubic centimeters; there were no cells, and the Wassermann reaction was negative. Roentgenograms of the cervical portion of the spine showed slight thinning of the pedicles of the third, fourth and fifth vertebrae.

Course.—Because the neurologic symptoms were, and had been, all referable to a single lesion in the cervical portion of the spinal cord and the spinal fluid protein was consistently elevated at the time of the paralysis, it was decided to make a myelographic examination. An ovoid defect was visualized when the "pantopaque" (an iodized poppyseed oil with special adhesive properties) reached

the level of the fourth cervical vertebra (fig. 2). A laminectomy was performed on Jan. 22, 1946 and exposed a grayish mass lying under the dura on the right dorsilateral surface of the spinal cord. It was surrounded by a thin membrane, as though the arachnoid had split to encompass it. Dorsally the tumor and membrane were so tightly adherent to the dura that part of the dura was removed with the tumor. The tumor was fluctuant and obviously cystic. Attached to the right anterolateral side of the tumor was a structure having the appearance of a nerve root filament, but it was not sensitive to manipulation like the other nerve roots. Although it seemed to leave the canal with the other filaments of the fourth cervical nerve root, it first made a detour caudal to the attachment of the dentate ligament at that level, whereas the other filaments

Fig. 2.—Lateral view of the cervical portion of the spine, showing the cyst at the fourth cervical vertebra outlined with "pantopaque."

passed cephalad to the attachment. There was no evidence that this structure passed through the tumor and joined the spinal cord, and it was therefore regarded as a pedicle of the tumor attaching it to the dura. The tumor measured 2 by 2 by 1 cm. and compressed the spinal cord. This cystic mass was completely removed, without rupture of the wall.

The patient's postoperative course was uneventful, and within a few days he began to improve. He was discharged from the hospital one month after operation, being able at this time to walk with slight assistance but still showing considerable weakness and spasticity in all extremities.

Pathologic Observations.—The wall of this cyst was semitransparent and grayish white. It was composed of rather tough fibrous tissue. The contents of

the cyst were fluid and tended to string out as mucinous material does; this material was grayish white. A smear of the contents of the cyst showed only amorphous material, containing a few poorly preserved cells. The material gave positive chemical reactions for mucin. Microscopic section of this cyst revealed

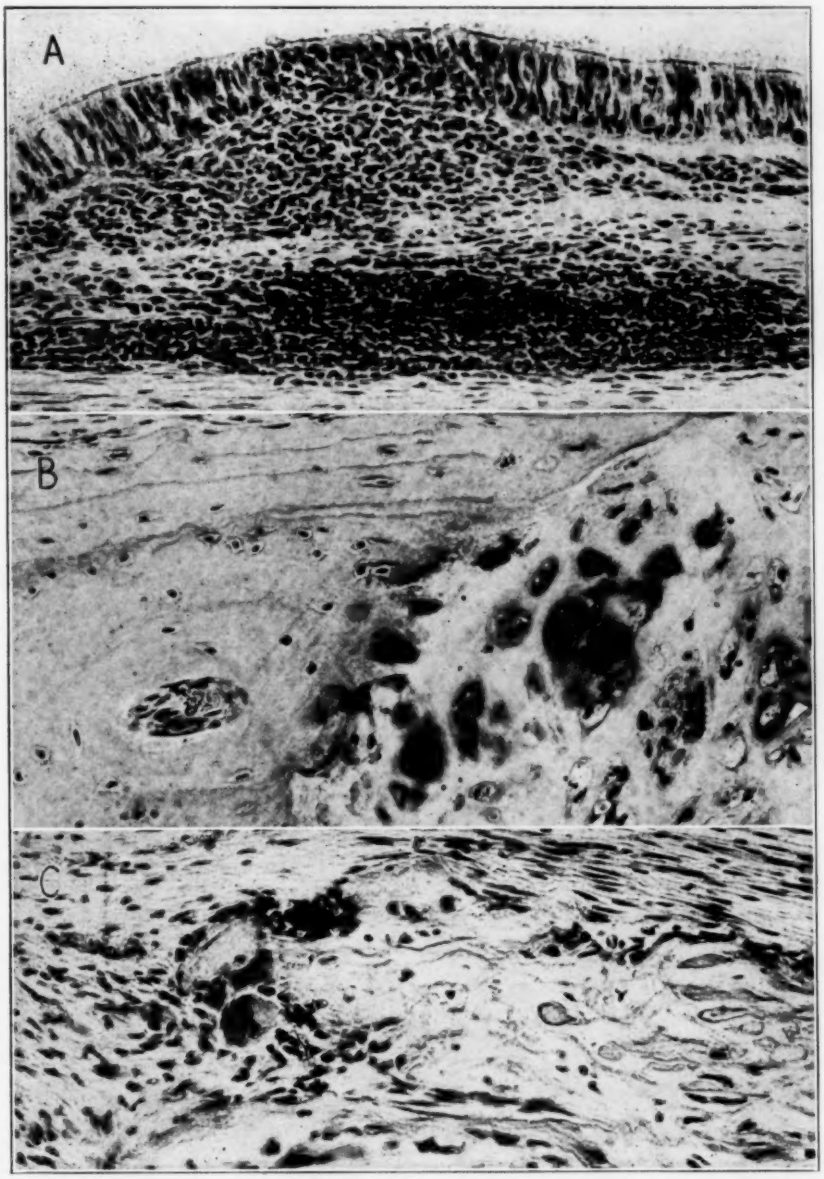

Fig. 3.—Photomicrograph of the wall of the cyst, showing (*A*) ciliated columnar epithelium and focus of lymphocytes in the wall of the cyst, (*B*) hyaline cartilage and bone beneath the epithelial lining of the cyst and (*C*) mucinous material in the wall of the cyst, surrounded with macrophages and foreign body giant cells.

that the wall was composed of collagenous connective tissue and, in places, bone and cartilage. Grayish, mucinous material surrounded by macrophages and foreign body giant cells (fig. 3 *C*) could be seen in some parts of the wall. At one place

a nerve twig could be seen within the wall of the cyst. The lining was composed of a columnar, ciliated epithelium. Just beneath the epithelium there were focal collections of lymphocytes and macrophages. With the phosphotungstic acid stain there were no glial fibrils. The total thickness of the wall of the cyst was from 0.5 to 1 mm.

Diagnosis.—The diagnosis was teratomatous cyst of the spinal meninges.

COMMENT

The Clinical Syndrome.—The outstanding clinical features of these 2 cases were the intermittent pain and the paralysis. In case 1 there were five attacks of pain in the lumbar portion of the back, in two of which there were weakness of the legs, sensory impairment and partial paralysis of the bladder and rectum. In the second case there were five attacks of cervical pain, followed by hemiplegia or quadriplegia with sensory paralysis and paralysis of the bladder and rectum. In each attack the symptoms were of subacute onset and development progressed to a certain point, and the process then underwent fairly complete recession. Between attacks, even though the paralysis had been almost complete, the patient was almost entirely free of symptoms.

The clinical syndrome was essentially that of a transverse lesion of the cord of reversible character, in the thoracic region in 1 case and in the cervical region in the other. The distribution of motor and sensory paralysis was the same in each attack. One side was always affected more than the other, and in case 2 the pattern of motor involvement was always in the order of the right arm, right leg, left leg and left arm. When the paralysis was incomplete a partial Brown-Séquard syndrome was present. The recovery from sensory and motor paralysis was always in reverse order; i. e., the parts last paralyzed were the first to move. Motor symptoms usually preceded sensory symptoms and, if the attack was not very severe, were the only symptoms present. Recovery from motor paralysis was always slower than that from sensory paralysis. In case 1 there was a tendency toward segmental sensory dislocation in the last attack; the loss of pain and temperature sensibility was greater over the lower thoracic and lumbar segments than over the sacral ones. Touch sensation was always affected less than pain and temperature sense. The bladder and rectum were paralyzed only when motor paralysis involved both sides of the body.

Pathophysiologic Changes.—In these cases, particularly in case 2, there were manifested in an almost perfect natural experiment the effects of hydrodynamic compression of the spinal cord. This caused pain over the spine, probably due to stretching of the meninges, and in case 2 root pain. One side of the cord was observed to be compressed more than the other, accounting for the asymmetry of the sensory and motor paralysis and the partial Brown-Séquard syndrome. The increased spinal fluid protein and the partial dynamic block in

case 1 were caused by obstruction of the spinal subarachnoid space. In case 2, even though there was a high protein content, the cyst was so soft that it transmitted the intracranial pressure.

The cause of the intermittent swelling of the cysts is an intriguing problem. Four possible explanations occur to us: 1. The wall of the cyst ruptured when the pressure reached a certain point, and the contents escaped into the subarachnoid space. 2. The wall of the cyst broke under the increasing pressure of accumulated secretions, and the contents of the cyst escaped into the wall of the cyst, being removed by macrophages and giant cells. 3. The mucinous contents were resorbed by the same cells which secreted them. 4. The cystic fluid was in osmotic relation to the blood and was therefore influenced by hemodilution or by congestion of meningeal vessels of whatever cause, and possibly by other factors. The first possibility seems unlikely because the wall of the cyst was tough and because there was at no time any meningeal irritation, as would be expected from a sudden escape of mucinous secretion into the subarachnoid space. Although the presence of macrophages and giant cells around homogeneous material in the vessel wall supports the second hypothesis, it seems improbable to us that the cyst could be effectively decompressed by this means. The most plausible explanation is that the rate of mucinous formation and absorption is influenced by hydration of the blood or by congestion of meningeal vessels. It is interesting in this connection that in case 2 the last three attacks were preceded by an infection of the respiratory tract. Swelling of cerebral tumors and of cerebral cysts before the menstrual period and with infection has been observed and commented on by numerous authors. Our pathologic material does not permit a final decision on this matter.

The differential diagnosis of an intermittent solitary lesion of the spinal cord includes relatively few diseases. Acute myelitis or multiple sclerosis can, of course, produce over a relatively short period symptoms referable to the spinal cord which will undergo spontaneous remission. This was the diagnosis entertained for a year or two in the second case. If, however, one insists on the cardinal criteria of multiple sclerosis, namely, that the lesions be disseminate in their distribution as well as discontinuous in time, this diagnosis cannot be validated. Further, the extremely high protein content of the spinal fluid and, in the first case, the dynamic block with each exacerbation of the disease are not seen in cases of multiple sclerosis. A ruptured cervical or thoracic disk may at times compress the cord intermittently. Cases have been reported in which after each of several successive traumas to the spine symptoms referable to the spinal cord have been produced, only to subside on immobilization of the spine. The spontaneous nature of the symptoms in our cases and their subacute evolution

in each attack were decidedly against this possibility. Spinal adhesive arachnoiditis may at times cause symptoms which progress up to a point and then undergo partial remission, only to recur with a subsequent infection. This was the diagnosis most seriously considered in the first case. However, the discreteness of the lesion and the complete remission of symptoms between attacks tended to exclude both this disease and multiple sclerosis. The second objection could also be raised against an aneurysm of the anterior spinal artery. Repeated dislocation of the atlas on the axis, which may occur in young people and cause compression of the cervical portion of the cord with sensory and motor paralysis and respiratory difficulty, may simulate a spinal meningeal cyst. In our cases the lower level of involvement of the spinal cord and the normal appearance of the spine in lateral roentgenograms excluded this condition. Syringomyelia and myelodysplasia were suggested by the sensory changes in case 1, but the intermittent course of the disease justified rejection of this possibility.

Origin of the Cysts.—The genesis and classification of cysts of this character regardless of their location have been subjects of much speculation. Many observers have pointed out the similarity of the lining of ciliated columnar epithelium to the epithelium of the respiratory tract and the fetal gut, or even to fetal ependyma. The representation of tissues derived from the ectodermal and mesodermal germ layers indicates that these tumors are not the result of mechanical displacement of ectodermal elements during fetal life, such as occurs in the dermoid or epidermoid tumors but, rather, are complex teratomatous neoplasms caused by a dislocation of pluripotential cells during early embryonic life. This explanation has been accepted by Kubie and Fulton,[1] by Hosoi[2] and by Bucy and Buchanan[3] and seems most plausible. The relationship between these cysts and myelodysplasia or other defects in closure of the neural tube is unsettled. Because of the absence of obvious connection with the spinal cord in some cases and the absence of glial elements in the wall of the cyst, we prefer to view these tumors as true teratomas which may in some instances be associated with a congenital malformation of the spinal cord.

Review of the Literature.—We have found 6 other cases in the medical literature which closely resemble the 2 cases reported here. Seven additional cases are described in the publications of Gowers and

1. Kubie, L. S., and Fulton, J. F.: Clinical and Pathological Study of Two Teratomatous Cysts of Spinal Cord, Containing Mucus and Ciliated Cells, Surg., Gynec. & Obst. **47**:297-311 (Sept.) 1928.

2. Hosoi, K.: Intradural Teratoid Tumors of Spinal Cord: Report of Case, Arch. Path. **11**:875-883 (June) 1931.

3. Bucy, P. C., and Buchanan, D. N.: Teratoma of Spinal Cord, Surg., Gynec. & Obst. **60**:1137-1144 (June) 1935.

Horsley,[4] Gerlach,[5] Forbes,[6] Frick,[7] Thomas and Quercy,[8] Bielschowsky and Unger[9] and Hansmann[10] of teratomas of the spinal cord, but they differed in that the tumors were not cystic, did not produce symptoms intermittently and were in some instances associated with myelodysplasia.

In 1928 Kubie and Fulton[1] described in detail 2 cases of teratomatous cyst of the spinal cord which was successfully removed at operation. The cyst in each case was solitary, was situated in the spinal subarachnoid space without attachment to the spinal cord, was lined with a ciliated columnar epithelium and had in its wall mucous and serous glands, smooth muscle, nerve fibers, bone and cartilage. Case 1 was that of a child aged 2 years who had weakness of the right leg and a "tender" abdomen. Roentgenograms disclosed occult spina bifida of the lower thoracic, lumbar and sacral vertebrae. With lumbar puncture between the tenth and the eleventh thoracic vertebra, a thick, "egg-white" fluid filled with ciliated cells was obtained. At operation a large flattened cyst was observed extending from the tenth dorsal to the fourth lumbar vertebra. The child recovered completely. Case 2 was almost exactly like our second case. The patient, a white woman aged 27, had had five attacks of left hemiplegia with pain in the left cervical region and the Brown-Séquard type of dissociation of sensation in the trunk and extremities at varying intervals since the age of 21. In her last attack there was almost complete quadriplegia with an upper level of sensory disturbance at the fourth cervical dermatome and grave embarrassment of respiration. At operation a cyst was observed attached to the meninges of the cord at the fourth cervical segment on the left side. The authors expressed the belief that both cysts were congenital and probably represented ependymal diverticula of the spinal cord.

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4. Gowers, W. R., and Horsley, V.: A Case of Tumor of the Spinal Cord: Removal; Recovery, Med.-Chir. Tr., London **71**:377-430, 1888.

5. Gerlach, W.: Ein Fall von congenitaler Syringomyelie mit intramedullärer Teratombildung, Deutsche Ztschr. f. Nervenh. **5**:271-301, 1894.

6. Forbes, J. G.: Intra-Medullary Teratoma of the Spinal Cord, St. Barth. Hosp. Rep. (1905) **41**:221-232, 1906.

7. Frick, K.: Ueber ein Teratom des Rückenmarkes, Frankfurt. Ztschr. f. Path. **7**:127-134, 1911.

8. Thomas, A., and Quercy: Syringomyélie, hyperplasie due tissu conjonctif, fibres musculaires striées dans la moelle, Nouv. iconog. de la Salpêtrière **25**:364-383, 1913.

9. Bielschowsky, M., and Unger, E.: Syringomyelie mit Teratom- und extramedullärer Blastombildung: Zur Kenntnis der Pathogenese der Syringomyelie, J. f. Psychol. u. Neurol. **25**:173-218, 1920.

10. Hansmann, G. H.: Congenital Cystic Tumor of Neurenteric Canal with Special Reference to Its Histology and Pathological Significance, Surg., Gynec. & Obst. **42**:124-127 (Jan.) 1926.

Hosoi,[2] in 1931, described with full clinical details a case of intradural teratoid tumor of the spinal cord in the lumbar region. There was occult spina bifida at the fifth lumbar level. The patient gave a vague history of transient paralysis of the legs during childhood, after which he was well until the age of 25, when over a period of two to three weeks there developed pain in the back, weakness of the legs, sensory impairment in one leg and urinary and fecal retention. There were dynamic block of the cerebrospinal fluid and xanthochromia with a very high protein content. Most of the tumor was removed, and the patient recovered almost completely within a few months. Microscopic sections of the tumor revealed smooth muscle cells, fibrous connective tissue, numerous mucous glands and pacinian corpuscles.

In 1934 Puusepp [11] reported a case of teratoma of the spinal cord that was almost exactly like the second case of Kubie and Fulton and our second case. The patient was a young adult who had had several isolated attacks of pain in the neck, motor and sensory paralysis in all four extremities and sphincteric disturbances between the ages of 5 and 27 years. A cystic tumor of the spinal meninges in the cervical region which was attached to the dura was successfully removed.

Bucy and Buchanan,[3] in 1935, described a teratoma occurring in an infant 16 months of age. The only symptoms were irritability, anorexia and slowly developing paraplegia. The cerebrospinal fluid was yellow, contained abnormally large amounts of protein and clotted spontaneously (Froin's syndrome). Laminectomy disclosed a cyst beneath the dura and compressing the spinal cord from the eleventh dorsal to the fourth lumbar vertebra. The cyst was filled with thick, tenacious, glairy material. At one point the cyst appeared to be attached to the dorsal surface of the spinal cord. Microscopic sections of the cyst showed that it was lined with ciliated cuboidal epithelium and goblet cells, and in a mural nodule there were hyaline cartilage and mucous glands.

Masten,[12] in 1940, reported another case in which a cystic teratoma of the spinal cord was observed at operation. The patient, a 5 year old girl, had had pain in the neck and arms and stiffness of the neck for three weeks and had right hemiparesis affecting the arm and leg on the day of admission. Sensation could not be tested. There were a partial dynamic block of the cerebrospinal fluid and a total protein of 1,200 mg. per hundred cubic centimeters. Operation revealed a cystic tumor beneath the dura from the fourth cervical to the first

11. Puusepp, L.: Variété rare de tératome sous-dural de la région cervicale (intestinome); quadriplégie; extirpation; guérison complète, Rev. neurol. **2**:879-886 (Dec.) 1934.

12. Masten, M. G.: Teratoma of Spinal Cord, Arch. Path. **30**:755-761 (Sept.) 1940.

dorsal vertebra. During its removal the cyst ruptured and a grayish, sticky fluid was discharged. The patient died on the third postoperative day of bronchopneumonia. Postmortem examination revealed evidence of compression of the spinal cord. There is no mention of any congenital abnormality of the spinal cord, though the neurosurgeon thought that the tumor was attached to the dorsal surface of the cord.

SUMMARY

Two unusual cases of intermittent compression of the spinal cord by a teratomatous cyst in the meninges are described. Case 1 was that of a white man aged 41 who had had five attacks of pain in the back and partial paraplegia with sensory loss and sphincteric disorder. Case 2 was that of a white man aged 29 who had had five attacks of pain in the neck followed by hemiplegia or quadriplegia, sensory impairment below the lesion, paralysis of the bladder and rectum and respiratory embarrassment. The cerebrospinal fluid protein was increased, and in case 1 there was a dynamic block. In case 1 the cyst was partially removed, and in case 2 it was completely removed, with excellent therapeutic results in both. Microscopic examination of the cysts established their teratomatous nature.

The clinical syndrome is unique. We know of no other spontaneous lesion which will produce compression of the spinal cord intermittently. However, this condition has been mistaken in some instances for ruptured cervical disk, recurrent atlantoaxial dislocation, multiple sclerosis and chronic adhesive arachnoiditis. The mechanism of production of symptoms is swelling of the cyst and compression of the spinal cord. The origin of the cyst is thought to be a displacement of pluripotential cells during early embryonic life and the formation during childhood or adult life of a benign tumor composed of several different structures.

818 Harrison Avenue.

Clinical Notes

PHOTIC DRIVING AS A CAUSE OF CLINICAL SEIZURES IN EPILEPTIC PATIENTS

STANLEY COBB, M.D., BOSTON

The effect of visual stimuli on the electroencephalogram has been of interest since the earliest work on cerebral potentials. Berger noted changes in alpha rhythm following retinal stimulation. Walker [1] and others have studied the effect on the electroencephalogram of intermittent photic stimulation of the retina. The electroencephalogram obtained from the occipital cortex may take on a frequency synchronous with the flicker. This is called photic driving. Moreover, Walker and his associates stated:

> . . . If intermittent photic stimuli are allowed to fall suddenly on the retina, one encounters a peculiar hump and spike arrangement which persists for the first six or eight stimuli, after which the waves assume a more sinusoidal form. This peculiar hump and spike formation may be seen at almost any frequency, but is particularly well demonstrated when the frequency of the intermittent photic stimulus is approximately 6 per second.[1]

Figure 10 of the paper by Walker and co-workers shows these "spike and hump" responses. They bear a remarkable resemblance to the common wave form of the electroencephalogram in cases of petit mal when short lapses of consciousness appear. It was thought that this resemblance made pertinent 3 clinical observations in which epileptic patients had experienced a lapse of consciousness after exposure to flickering light.

CASE 1.—A girl aged 17 was admitted to the Boston City Hospital in January 1931 with the complaint of "lapses" in which she lost contact for a few seconds. She first noticed these spells at the age of 11, and they gradually became commoner and severer. When she was 13 other people noticed them, and at school she was teased for "absent mindedness" and was nicknamed "lapsey." She had had one convulsive seizure in which she fell, bit her tongue and lost consciousness for five minutes. This occurred two weeks prior to admission and was ushered in by an unusual series of her petit mal attacks. When quiet and at peace she has few attacks; when disturbed by emotional stress, as at dances or examinations, she is likely to have many. She has noticed that flickering light bothers her and is likely to bring on repeated petit mal seizures. For example, leading up to a house which she frequently visits is a long avenue flanked by tall trees arranged in rows. When the sun is low and slanting through the trees any one riding up the avenue in an automobile is exposed to flickering light. This situation has several times caused the patient to have repeated petit mal attacks, culminating in a dazed state when she reached the house.

From the Department of Neuropathology, Harvard Medical School, and the Department of Psychiatry, Massachusetts General Hospital.

1. Walker, A. E.; Woolf, J. I.; Halstead, W. C., and Case, T. J.: Photic Driving, Arch. Neurol. & Psychiat. **52**:117 (Aug.) 1944.

CASE 2.—A woman aged 50, of superior intelligence and education, came to my office in January 1944 to talk to me about her epileptic niece. She has a sister with migraine. After discussing the niece, she asked me about herself, saying: "I myself have had one convulsion, a few hours after my son was born. Never before nor since; but I had a peculiar experience once. I was standing outside a village store in the evening. The arc light overhead suddenly began to flicker. It went on and on. I felt queer, and suddenly my vision was wiped out. I did not know where I was or what was happening for a few seconds. I did not fall; I just went blank for a short while."

CASE 3.—A clerk of 33 came to the office in May 1946 with the complaint of epileptic fits occurring about once a month at night. A careful history revealed that he had a severe head injury at the age of 13. He had a "spell of unconsciousness" about a year later and another at the age of 16. He was then given phenobarbital and had no seizures until the beginning of the present illness. When pressed to be exact, he said: "Well, I had two funny spells in college at about the age of 19." He experimented in a physics laboratory with a light that gave interrupted flickers at a rapid rate. While working with this, he twice began to feel confused and then went into a short period of unconsciousness without convulsive movements. His electroencephalogram in 1946 showed some low voltage waves at 6 per second frequency.

These clinical observations suggest the importance of investigating the effect of flickering light on epileptic patients, using various rates of flicker for patients with various types of electroencephalograms.

Massachusetts General Hospital.

Obituaries

JOHN FAVILL, M.D.

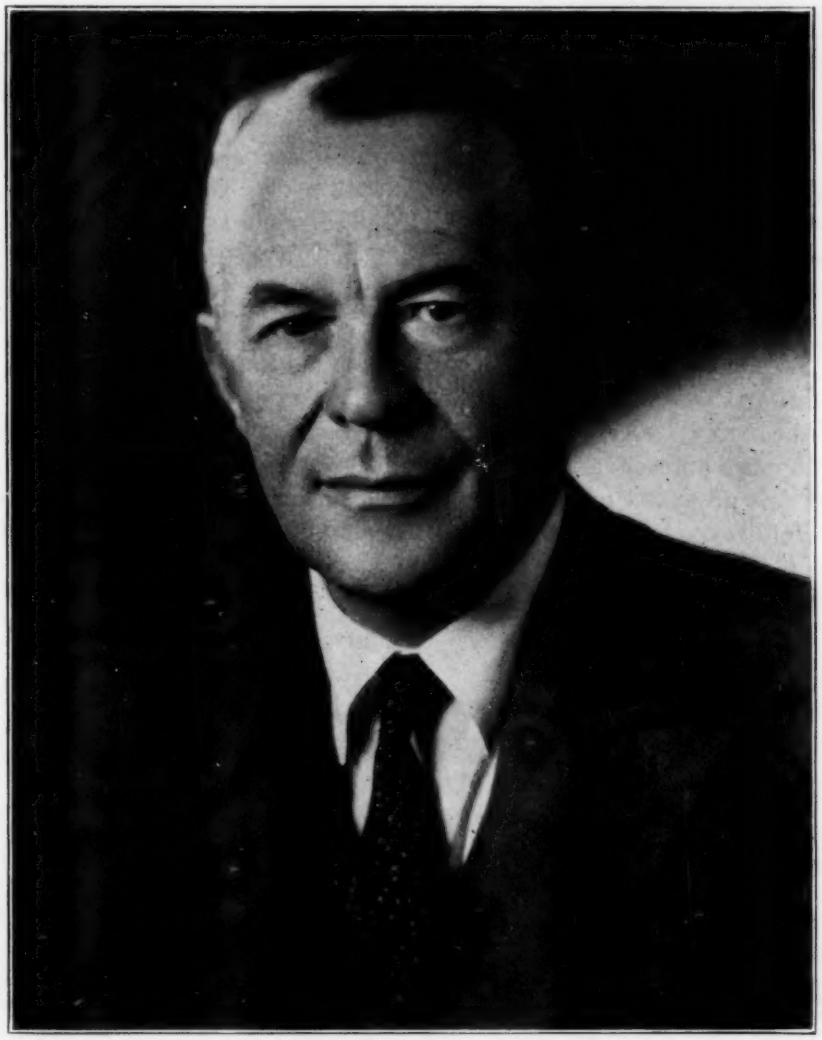
1886-1946

Dr. John Favill was born Sept. 9, 1886, at Madison, Wis., to Dr. Henry Baird Favill and his wife, Susan Pratt Favill. On the maternal line there were many generations of New Englanders, and on the paternal side there was the heritage of generations of colonial English, to which the blood of an Ottawa Indian chieftain had entered some five generations before him. There was something of the Indian in John Favill. It was evident not only in the prominent cheekbones and the suggestion of native coloring, but also in the softness of his step, his slowness to speak, his freedom from verbosity and his love of and interest in the laws of the natural universe. Both father and son were proud of this heritage.

The Favill family moved to Chicago in 1894, where John completed his preparatory education. From 1894 to 1900 he attended Cobb's School. He graduated from Coultier's University School in 1905. His college education was completed at Yale in 1909. He studied medicine at Harvard Medical School, from which he graduated *cum laude* in 1913. After an internship at Massachusetts General Hospital, Dr. Favill returned to Chicago to associate himself with his father in the practice of internal medicine, being licensed to practice in 1915. In 1917 he was commissioned a first lieutenant in the Army Medical Corps and served chiefly with United States Base Hospital no. 14, the unit from St. Luke's hospital, where he had been a member of the staff. It was during his military service that his interest in neurology was stimulated, so that after his return he entered actively into this field of medicine. He was discharged from the Army in 1919, having received the rank of captain. While Dr. Favill was unable to take an active part in World War II, much of his effort was spent in preparation for such service.

To his profession and his chosen specialty he gave his efforts. On his return to Chicago, he became a member of the staff of St. Luke's Hospital and began his long career of teaching at Rush Medical College. In recognition of his efforts in the hospital, he rose to be senior neurologist in 1928 and held executive positions on the staff. In 1937 he transferred his hospital connections to the Presbyterian Hospital. Here he was attending neurologist and psychiatrist until his death, becoming

chief of the division in 1945. His ability as a teacher brought him recognition. Beginning as an assistant in medicine in 1915, he attained the rank of professor of neurology in 1934, which rank he continued to hold when Rush Medical College became associated with the University of Illinois. In 1921 he became a member of the neurologic



JOHN FAVILL, M.D.
1886-1946

staff of Cook County Hospital. Here he served continuously until 1937, and during his last two terms was chief of the section. He also served as consultant to the Institute for Psychoanalysis and the Highland Park and Lake Forest Hospitals.

Dr. Favill took an active part in the various associations having to do with the fields he was interested in. In many of these associations he was honored with executive positions. He was president of the Chicago Neurological Society from 1926 to 1928, president of the Chicago Society for Personality Study from 1936 to 1937, president of the Central Neuropsychiatric Association in 1937-1938 and president of Medical Unit Commander's conference in 1937-1938. He held membership in the American College of Physicians, the American Neurological Association, the American Psychiatric Association and the Association for Research in Nervous and Mental Disease.

To the field of medicine he contributed three books, "Outline of the Cranial Nerves," 1933; "The Relationship of Eye Muscles to Semicircular Canal Currents in Rotationally Induced Nystagmus," 1936, and "Outline of Spinal Nerves," 1946. In 1917 he published a memorial volume to his father, "Henry Baird Favill; Life, Tributes and Writings."

While neurology was his chosen field and he won recognition in it, his efforts were not confined to it. In 1924 he was commissioned major in the Army Reserve Medical Corps. With quiet and ceaseless effort he applied himself to the study of the problems of military medicine. He was promoted to the rank of lieutenant colonel in 1931 and to that of full colonel in 1938. From 1939 to 1942 he was Commanding Officer of United States General Hospital 114. In 1942, because of illness, he was placed on the inactive list.

His interest in mathematics led him into the study of navigation. In the September 1935 issue of the *Naval Institute Proceedings,* he published a new method for determining latitude. This gained for him the esteem of many old and seasoned navigators. Encouraged by this, he continued the study, and in 1940 he published "The Primer of Celestial Navigation." This book was to go through three editions and was a true contribution to the better understanding of the subject. It was used extensively in preparation of navigators during the last war. Not content with writing about navigation, he prepared himself, took the examination and won a certificate as navigator, United States Power Squadron. It is perhaps ironic that he suffered from seasickness and had no interest in sailing.

In the later years his search for knowledge took him more and more into the field of philosophy. At the time of his death he was compiling his contributions. He was interested in psychic research. While he had no brief for psychic cults, or for the idea of communications with the spirit world, to him the phenomenon of our awareness was still a mystery, and he believed that if one worked and studied the truth regarding it might sometime be recognized.

In relation to his nonmedical activities, he took membership in the American Society for Psychic Research, the American Legion, the Veterans of Foreign Wars, the Reserve Officers Association, the American Unitarian Association, the National Dairy Association, the Naval Institute and the United States Power Squadron.

He was a member of the University, the Saddle and Cycle, the Cliff Dwellers, the Wayfarers, the Army and Navy and the Commonwealth Club.

On June 20, 1917 John Favill was married to Rhea Statcup of New York city. This marriage was dissolved in 1934. He married Alice M. Wells on May 31, 1935. A daughter, Elaine, was born May 9, 1936.

Dr. Favill attended the Association for Research in Nervous and Mental Disease in December 1946, fully aware of the state of his health. He died of coronary thrombosis on Dec. 21, 1946, the day following his return.

The contributions made by Dr. Favili in his many fields of endeavor will speak for themselves and will reveal the quality of the man. The philosophy that guided and urged him on and the manner in which he carried out his ideas may be of greater interest. In his presidential address, "The Great Delusion," before the Central Neuropsychiatric Association, he exposed his philosophy and his confession of faith. He believed in Truth, not as something that one manufactures but as "some sort of a non-material reality." This truth had through the ages broken through to our awareness. Since this was the philosophy he believed in, then his "supreme function" was the recognition of Truth. To this end he must continually and persistently prepare himself. Not only did Dr. Favill believe in these concepts; his life bears out the fact that he carried them out. He must always master the details of any subject to which he turned his efforts. Not only must he learn the facts, but he must do everything he could to clarify them, so that they might be more simply stated and more easily perceived by others. His lectures were always revised, the nonessentials discarded and new facts added. His efforts in military medicine and in navigation were similarly characterized. He worked so quietly and unobserved that he almost got a reputation for being indolent. Quite the contrary, he was a ceaseless worker. Some of his work was conceived and planned when confined to bed. He always took his problems with him when on vacation. He utilized nearly every available hour to prepare himself for the "recognition of Truth." Bearing in mind his near worship of truth, one can understand his inherent distrust in any structure based on misconception, and also see why he had so much interest in mathematics. He always endeavored to reduce his problem to a mathematical equation, for there he felt secure in his reasoning. When discussing the

relationships of ocular muscles to the semicircular canal currents in rotationally induced nystagmus, he proved his thesis by an algebraic equation. Perhaps the work which brought him his greatest recognition was in the field of mathematics, namely, navigation. Interesting and characteristic of the man, it was not his love of the sea that gave him the impetus to study navigation; it was his love of facts and his struggle to prepare himself to recognize them. He will be remembered not only for what he did but for how he accomplished it.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Physiology and Biochemistry

FUNCTIONAL CHANGES IN NERVE AND MUSCLE AFTER PARTIAL DENERVATION. H. M. HINES, W. H. WEHRMACHER and J. D. THOMSON, Am. J. Physiol. **145**:48 (Nov.) 1945.

Hines, Wehrmacher and Thomson studied the effects of partial denervation on the gastrocnemius muscles of rats and cats. Partial denervation was obtained by section of the fourth and fifth spinal nerves in the rat and of the seventh lumbar nerve in the cat. At various times after partial denervation determinations were made of muscle weight and of isometric tension responses to direct stimulation and to stimulation of the tibial nerve. These determinations were controlled by observations on the contralateral (normal) extremities. Isometric tension responses were considerably decreased three days after partial denervation, but the tension responses nine, fourteen and fifty days after partial denervation were much more forceful than at the end of three days. This improvement in response was not considered the result of recovery from shock and trauma, nerve regeneration or recovery from weakness in the control extremity but was thought to result from hypertrophy of nondenervated muscle fibers and extension or unmasking of peripheral neuromuscular terminals.

FORSTER, Philadelphia.

AGE, SEX, CARBOHYDRATE, ADRENAL CORTEX AND OTHER FACTORS IN ANOXIA. S. W. BRITTON and R. F. KLINE, Am. J. Physiol. **145**:190 (Dec.) 1945.

Britton and Kline studied the effects of low barometric pressures on experimental animals. Age, sex, species and environmental temperature were important factors in resistance to low barometric pressures. Rat fetuses and immature pouch opposums were highly resistant to anoxia. The high resistance declined rapidly in infant animals during the first one or two weeks after birth, and for a period the young animals were more susceptible than adults. The superior resistance of young animals may be due to the relatively large size of the adrenal glands, and the high glycogen content of the liver. Of the mammalian types studied, the American brown bat had the highest resistance. The female animals were more resistant to anoxia than the males. This, too, may be due to the relatively larger adrenal glands of females. The influence of the adrenal glands is further indicated by the absence of variation between the sexes in infancy, when the adrenal glands are of approximately equal size in the two sexes. The survival time under anoxia was inversely related to the environmental temperature. The resistance of rats to low barometric pressure was greatly augmented by the administration of carbohydrates, while the administration of insulin decreased tolerance to anoxia. Resistance to anoxia could be increased by inhalation of a mixture of carbon dioxide and oxygen and injection of dextrose solution. Exposure to anoxia did not alter serum levels of potassium, sodium and chloride. Britton and Kline conclude from their data that the adrenal cortex aids greatly in extending life under anoxic conditions.

FORSTER, Philadelphia.

FRACTIONATION OF LECITHINS AND CEPHALINS. E. A. WELCH, J. Biol. Chem. **161**:65, 1945.

The lecithins and cephalins are complex mixtures of chemical entities, differing from each other (*a*) in their component fatty acids; (*b*) in the case of the cephalins,

in the nitrogenous constituent, and (*c*) in the point of substitution of the phosphoric acid–base group in the molecule. A procedure is presented for the fractionation of the α and β isomeric forms of lecithin and cephalin. With use of this method, it was found that in brain the α forms predominate and in the heart and liver α-lecithin and β-cephalin predominate.

PAGE, Cleveland.

A METHOD FOR THE DETERMINATION OF DESOXYRIBONUCLEIC ACID, RIBONUCLEIC ACID, AND PHOSPHOPROTEINS IN ANIMAL TISSUES. G. SCHMIDT and S. J. THANNHAUSER, J. Biol. Chem. **161**:83, 1945.

The methods used at present for the determination of the higher nucleic acids in organs are based on certain color reactions of their carbohydrate components. The quantitative evaluation of these color tests gives satisfactory results with the free carbohydrates and with the purine nucleosides and nucleotides. Application of the color tests to the higher nucleic acids, however, encounters some serious difficulties, which arise mainly from the resistance of the pyrimidine nucleotides against hydrolyzing agents, from the instability of desoxyribose and from the necessity of separating the nucleic acid from the proteins. An extensive discussion of these problems has recently been given by Davidson and Waymouth. It occurred to Schmidt and Thannhauser that these difficulties might be avoided if the quantitative estimations of desoxyribonucleic acid and of ribonucleic acid could be based on phosphorus determinations rather than on color tests of their carbohydrate components. The prerequisite for such a method would be the possibility of separating quantitatively the phosphorus fraction of ribonucleic acid from that of desoxyribonucleic acid. The separation of both phosphorus fractions can be achieved by the selective destruction of ribonucleic acid under the influence of a mild treatment with alkali. Rat brain was found to contain 15.1 desoxyribonucleic acid and 32.6 ribonucleic acid, expressed as milligrams of phosphorus in 100 Gm. of fresh tissue. Negligible amounts of phosphoproteins were found.

PAGE, Cleveland.

OXYGEN POISONING: V. THE EFFECT OF HIGH OXYGEN PRESSURE UPON ENZYMES: SUCCINIC DEHYDROGENASE AND CYTOCHROME OXIDASE. W. C. STADIE and N. HAUGAARD, J. Biol. Chem. **161**:153, 1945.

Experiments on the effect of oxygen at high pressure on succinic dehydrogenase, cytochrome oxidase and cytochrome c are reported. Oxygen at 7 atmospheres inactivates the succinic dehydrogenase of rat liver, kidney or brain. The rate of inactivation, however, is relatively slow. The succinic dehydrogenase activity of brain tissue of rats killed by oxygen at 7 atmospheres is not different from that of normal animals. Cytochrome oxidase and cytochrome c are unaffected by oxygen at 7 atmospheres. The significance of these findings in the general problem of oxygen poisoning is discussed.

PAGE, Cleveland.

OXYGEN POISONING: VI. THE EFFECT OF HIGH OXYGEN PRESSURE UPON ENZYMES: PEPSIN, CATALASE, CHOLINESTERASE, AND CARBONIC ANHYDRASE. W. C. STADIE, B. C. RIGGS and N. HAUGAARD, J. Biol. Chem. **161**:175, 1945.

The enzymatic activities of preparations containing pepsin, catalase, cholinesterase and carbonic anhydrase were determined before and after exposure to oxygen at high pressure. No significant changes were observed. Cholinesterase is an example of a sulfhydryl enzyme unaffected by oxygen.

PAGE, Cleveland.

OXYGEN POISONING: VIII. THE EFFECT OF HIGH OXYGEN PRESSURE ON ENZYMES: THE SYSTEM SYNTHESIZING ACETYLCHOLINE. W. C. STADIE, B. C. RIGGS and N. HAUGAARD, J. Biol. Chem. **161**:189, 1945.

The aerobic synthesis of acetylcholine by slices or homogenates of rat brain is unaffected by exposure to oxygen at high pressure. The choline acetylase activity of slices of rat brain is likewise unimpaired by excess oxygen. However, cell-free

preparations of acetylase are rapidly inactivated by oxygen. The relation of these findings to the problem of oxygen poisoning is discussed.

PAGE, Cleveland.

ANAEROBIC GLYCOLYSIS IN NERVOUS TISSUE. M. F. UTTER, H. G. WOOD and J. M. REINER, J. Biol. Chem. **161**:197, 1945.

A method is described for the preparation from the central nervous system of cell-free extracts and homogenates exhibiting high rates of anaerobic glycolysis. A study of the variable factors in the preparation of the extracts and homogenates has been made. Active extracts and homogenates have been prepared from spinal cord, medulla, cerebellum and cerebrum. For complete activity these preparations need, in addition to glucose and buffers, adenosine triphosphate, hexose diphosphate, diphosphopyridine nucleotide, magnesium ions and nicotinamide. Evidence is presented that the "inhibitor" of brain extract reported by Geiger is a diphosphopyridine nucleotidase. Inhibition of the nucleotidase can be obtained with nicotinamide or by incubation of the preparation with diphosphopyridine nucleodide and bicarbonate buffer. Etherization of animals prior to preparation of glycolytic extracts and homogenates did not have any detectable effect on extracts and had slight or no effect on homogenates. The preparations have approximately linear activity with time and with increasing concentration of tissue for sixty minutes or longer. They, therefore, should prove useful in the assay of enzymes of anaerobic glycolysis of the central nervous system.

PAGE, Cleveland.

PHOSPHORUS COMPOUNDS IN ANIMAL TISSUES: I. EXTRACTION AND ESTIMATION OF DESOXYPENTOSE NUCLEIC ACID AND OF PENTOSE NUCLEIC ACID. W. C. SCHNEIDER, J. Biol. Chem. **161**:293, 1945.

The pentose nucleic acid content of rat brain was found to be 184 mg. per hundred grams of wet tissue, while the desoxypentose nucleic acid was 124 mg.

PAGE, Cleveland.

ST. LOUIS ENCEPHALITIS VIRUS IN BLOOD OF EXPERIMENTALLY INOCULATED FOWLS AND MAMMALS. W. MCD. HAMMON, W. C. REEVES and E. M. IZUMI, J. Exper. Med. **83**:175 (March) 1946.

Hammon and his collaborators state that of three species of mammals tested by peripheral inoculation (guinea pig, cat and horse) none showed viremia under conditions which suggested that any of these species would serve as a frequent source of mosquito infection. Of the birds tested (chicken, duck and dove) all showed viremia and might readily serve as natural sources of mosquito infection. Chickens were shown to be highly susceptible to infection with minute amounts of virus inoculated subcutaneously. Virus may appear in the blood of chickens within sixteen hours after inoculation, and it has persisted till at least the one hundred and twentieth hour. No fowl showed signs of illness as a result of the infection.

J. A. M. A.

LABORATORY TRANSMISSION OF JAPANESE B ENCEPHALITIS VIRUS BY SEVEN SPECIES (THREE GENERA) OF NORTH AMERICAN MOSQUITOS. W. C. REEVES, W. MCD. HAMMON, G. G. WOLF and C. ESPANA, J. Exper. Med. **83**:185 (March) 1946.

Reeves, Hammon and associates tested 10 common species of western North American mosquitoes for their ability to act as vectors of Japanese B encephalitis virus. Of the 10 species of mosquitoes tested, 7 were demonstrated to be laboratory vectors. These 7 species represent three genera (Culex, Aedes and Culiseta). Transmission was made to mice twenty-one times and to a chicken once. These results, in addition to the published accounts by Japanese and Russian workers of

the natural epidemiology of this disease, led the authors to believe that this virus might well establish itself in North America, especially if introduced in areas where native encephalitides are now endemic. These studies also indicate that species of mosquitoes (Culex tarsalis, Culex pipiens, Aedes dorsalis and Culiseta inornata) now known to be fully incriminated vectors of the western equine or St. Louis encephalitis viruses can also serve as laboratory vectors of the Japanese B encephalitis virus.

J. A. M. A.

EXPERIMENTS ON CELL AND AXON ORIENTATION IN VITRO: THE ROLE OF COLLOIDAL EXUDATES IN TISSUE ORGANIZATION. PAUL WEISS, J. Exper. Zool. **100**:353 (Dec.) 1945.

About 5,000 tissue cultures of Schwann cells and nerve fibers in liquid or clotted mediums, with and without the inclusion of fibers of various kinds and dimensions (glass, textiles and synthetic resins, from 8 to 500 microns in diameter) were observed. Conclusions were reached concerning the mechanisms of adhesion, orientation, locomotion and association of spindle cells and axons in vitro.

A colloidal exudate given off by explanted tissue fragments slowly spreads centrifugally over all exposed surfaces and coats them with a fibrous mat ("ground mat"). The terminal processes of spindle cells and axons adhere to and follow the ground mat even in liquid mediums.

Orientation of the fibrils of the ground mat may be produced in both liquid and clotted mediums by placing the explant against a groove exerting strong capillary action or in contact with glass or textile fibers. Subsequent movement of the tissue will follow this linear course.

Even if the circumference of the cylinder is several thousand times the width of the cell processes, there is a longitudinal arrangement of the fibrils as the exudate moves down the cylinder. Cells and axons migrating along such a surface have longitudinal orientation.

Cells that have made contact with fibers of glass or synthetic resins embedded in a plasma clot seldom leave the fiber and move back into the clot. Cells advance more than twice as fast and as far along a glass fiber as they do inside the surrounding plasma clot. The many intersections of the fibrin framework of the clot account for the difference in rates of advancement. The differences in "regeneration rates" of nerve fibers can be explained on the basis of the organization of their surroundings (scar tissue or oriented tissue) rather than on differences in rates of intrinsic activity of the neurons concerned.

Favorable conditions for the aggregation of cells and the fasciculation of nerve fibers are created by liquid spaces, whether primary or produced by proteolysis.

The experiments have reconfirmed the principle of "contact guidance" of spindle cells and nerve fibers and have shed light on the mechanisms of "thigmotaxis," or "stereotropism," in tissue formation. The morphogenic significance of fibrous exudates in development and wound healing has received wider support.

REID, Boston.

THE NERVOUS SYSTEM AND REGENERATION OF THE FORELIMB OF ADULT TRITURUS: IV. THE STIMULATING ACTION OF A REGENERATED MOTOR SUPPLY. MARCUS SINGER, J. Exper. Zool. **101**:221 (March) 1946.

Experiments were designed to isolate a regenerated motor supply and then to observe its influence on growth of the amputated limb. The results show that, although the normal isolated motor supply of a limb is incapable of supplying the neural influence necessary for regeneration of the limb, the neural requirements can be met by a regenerated complement of motor fibers. The observations suggested that a number of motor elements greater than the normal, as brought about during the course of motor reinvasion, is the important factor.

Since the neural factor essential for regeneration of the limb may be motor as well as sensory, Singer suggests that such neural activity is common to all nerve fibers.

REID, Boston.

SUSCEPTIBILITY TO POLIOMYELITIS. C. ARMSTRONG and D. J. DAVIS, Pub. Health Rep. **60**:710 (June 22) 1945.

Persons exposed to poliomyelitis may react quite differently, some having constitutional symptoms with paralysis while others harbor the virus but show no symptoms. The reason for this difference is unknown, as is the actual reason for the common occurrence of virus-neutralizing antibodies in serums collected from the general population. Approximately 70 per cent of patients with poliomyelitis form antibodies slowly, if at all, after a recognizable attack. If this neutralizing property is an inherited characteristic, it is possible that the fathers and mothers of patients with the paralytic form of poliomyelitis might be found to show a higher incidence of non-neutralizing serums than would persons of corresponding age from the general population. The serums for a determination of this point were collected from 42 mothers and 27 fathers of hospitalized patients with paralytic poliomyelitis in North Carolina during the 1944 outbreak. When tested with the Lansing strain of poliomyelitis virus in white mice, the serums from 39 mothers neutralized the virus, 3 partially neutralized it and none had no neutralizing action. Of serums from 27 fathers, 23 neutralized it, 3 partially neutralized it and 1 had no neutralizing action. These results give no indication that paralytic poliomyelitis is more likely to occur among those whose parents do not readily produce circulating antibodies against the virus.

J. A. M. A.

CAROTID SINUS AND RETINAL CIRCULATION. RISER and others, Presse méd. **53**:161 (March 31) 1945.

Riser and his associates report observations on 50 subjects in whom they determined simultaneously the retinal arterial tension and the general arterial tension while performing various manipulations on the carotid sinus, such as digital compression of the sinus region, inhibition of the sinus by procaine hydrochloride and compression of the carotid artery below the sinus. They stress that the variations provoked in the general and in the retinal arterial tension by excitation of the carotid sinus are always synchronous and of the same amplitude. There never appeared a direct action of the sinus on the retinal circulation that could be separated from the action on the general circulation.

J. A. M. A.

ELECTROPHYSIOLOGIC STUDIES ON METRAZOL EPILEPSY. P. CHAUCHARD and others, Presse méd. **53**:201 (April 21) 1945.

Chauchard and his associates found in experiments on rabbits, guinea pigs and rats that metrazol injections result in an inverse modification of the excitation time of the cerebral cortex (prolongation) and the peripheral nerves (shortening). The effects of metrazol on the nervous centers are complex. The investigations conducted by the authors confirm earlier observations which attribute to the base of the brain an important part of the metrazol attack, but they go further and bring proof that the cerebral cortex, far from being stimulated by metrazol, is depressed by it. This is in accord with the fact that in man the attack is accompanied by loss of consciousness, that is, by suppression of the cortical function. In the encephalogram, under the influence of metrazol the augmentation of voltage is on a par with a retardation of the waves, which speaks in favor of a depression. The authors show that the complex action of metrazol, depressing the superior centers and stimulating the inferior ones, must not be confounded with that of ordinary stimulants, such as strychnine, which excite the brain and the lower centers simultaneously. Great similarity exists in metrazol epilepsy, insulin coma and electric shock, which are used in psychiatry.

J. A. M. A.

Neuropathology

PROTOZOAN PARASITE OF CENTRAL NERVOUS SYSTEM. N. VEERARAGHAVAN, Indian J. M. Research **32**:207 (Oct.) 1944.

Veeraraghavan encountered forms in the midbrain of guinea pigs experimentally infected with rabies which have not apparently been previously described.

The peculiar forms have been investigated over the past six years. The conclusion was reached that they are due to the presence of a parasite, probably protozoal in character, which is specific to the central nervous system. It has not been possible to identify this parasite with any previously described, such as Encephalitozoon cuniculi, or with any known species of Toxoplasma. The protozoal parasite was first encountered in the midbrain of guinea pigs infected with the jackal strain of rabies virus. The parasite, with the exception of certain cystic forms of doubtful significance, invariably occurred in the cytoplasm of nerve cells, particularly those ventral to the central canal of the midbrain. In a few cases, parasites were observed also in the Purkinje cells of the cerebellum and in the hippocampus major. The smallest forms of the parasite encountered were minute "spores." They were regularly seen in the midbrain of the naturally infected dogs and jackals and in the brains of guinea pigs inoculated with suspensions of their brains. The next stage of the parasite appeared to be the "ring" form. It might be round or oval, and it was variable in its position within the vacuole. Certain forms resembling the *accolé* forms of the malaria parasite were occasionally noted. These consisted of a crescentic bridge of cytoplasm with a rounded chromatin dot. In slightly older forms the chromatin mass was slightly larger, the protoplasm was thickened and the parasite assumed a variety of shapes. Segmentation of the chromatin appeared to be the next stage in the development of the parasite. In the segmenting forms the protoplasm appeared to be a solid mass with a varying number of chromatin dots. No evidence was found to suggest that the various forms of the parasite were the result of alterations in the constituents of nerve cells. The possibility of the parasite being a natural infective organism common to dogs and jackals, and unconnected with rabies infection, was investigated. Neither parasites nor Negri bodies were ever encountered in animals without rabies. Certain stages in the life cycle of the protozoal parasite described appear to be "filtrable"; it has been possible to produce evidence of infection in experimental animals by the inoculation of suspensions of brain passed through Berkefeld V and N candles. The protozoal parasite appears to be specific to the central nervous system, and in spite of exhaustive searches it has never been observed in other organs and tissues. It was not observed except in association with natural or experimental rabies. The suggestion has been put forward that Negri bodies may represent a stage in the life cycle of the parasite.

J. A. M. A.

DYSTONIA MUSCULORUM PROGRESSIVA (TORSION DYSTONIA). C. DE LANGE, Ann. pædiat. **164**:169 (April) 1945.

Cornelia de Lange made microscopic studies of the brain, the greater part of the spinal cord and the visceral organs of a Jewish man who died at 45 and in whom the disorder began at the age of 8. The diagnosis of dystonia musculorum progressiva was verified by competent neurologists. The corpus striatum proved practically normal, but various parts of the brain and the cord presented anomalies which doubtless had a degenerative anlage. The author is of the opinion that in the cases of dystonia of idiopathic or degenerative type there exist no specific anatomic changes but that the disorder is the result of a disturbance in the dynamics of the brain, spinal cord, nerves and muscles. The basis of this disturbance might be a metabolic process which produces no changes that are microscopically demonstrable.

J. A. M. A.

Psychiatry and Psychopathology

SENILE PSYCHOSIS AND PELLAGRA. H. A. MEYERSBURG, New England J. Med. **233**:173 (Aug. 9) 1943.

Meyersberg says that several patients with psychoses of the senile type have been observed to improve after therapy with nicotinic acid, thiamine, riboflavin and substances rich in the vitamin B complex. Review of their records has shown that 2 had atypical pellagra. In the first patient, a woman aged 55, the late mani-

festations were like those of a vascular disturbance, although the earlier ones were neurasthenic. The latter disturbances, the memory defects and the confabulatory episodes resembled the Korsakoff syndrome, which may occur either in the senile psychoses or in pellagra. The episodes of stupor were similar to those described in pellagrins. The cutaneous lesions were those of riboflavin deficiency, and the mucosal alterations were the combined effect of several deficiencies. The response to treatment puts this case definitely in the pellagra group. The effect of nutritional inadequacy in a patient with a subclinical encephalopathy of the combined senile and vascular type was illustrated by the second patient, a man aged 78. The reestablishment of adequate neurologic function and the concurrent disappearance of the somatic signs of deficiency under therapy indicate that the neuropsychiatric dysfunction was related to biochemical imbalance. The neuropsychiatric manifestations of pellagra usually appear after dermal, oral or gastrointestinal manifestations have developed. In a small proportion of cases, however, neuropsychiatric signs alone are manifest. The senile pellagrous type of encephalopathy may respond well to treatment with crystalline vitamin B products or with natural vitamin B concentrates. The recognition of this group of cases may permit effective therapy. The maintenance of an optimal dietary by the normal aged person, as well as by the senile invalid, is of primary importance.

J. A. M. A.

Effects of Encephalitis Occurring During Childhood on Behavior and Personality: Study of 50 Cases. J. V. Greenebaum, L. A. Lurie, B. Leichtentritt and Florence M. Rosenthal, Ohio State M. J. **41**:1018 (Nov.) 1945.

Greenebaum and his associates report observations on 50 children who were referred to the Child Guidance Home because of behavior disorders and personality difficulties which were causally related to a previous attack of encephalitis. The patients were followed for from three to twenty-five years. The fact that there were 39 males and 11 females seems to indicate that males are more susceptible to disorders of this type than are females. The onset of the disease was predominantly early in infancy, in the majority of cases occurring before the age of 5 years. The onset of the behavior problems and personality changes occurred mostly below the age of 10 years. In the majority of the children the behavior and personality difficulties appeared immediately after the onset of the disease. The virus type of encephalitis predominated in this series. Neurologic abnormalities (pyramidal, extrapyramidal, ocular) were present in all but 9 patients. Five had grand mal, 2 petit mal and 4 paralysis agitans. The range in intelligence quotients was from 51 to 118. Only 14 were feebleminded. Of 20 children who were retested, 9 showed no change in the intelligence quotient, 1 showed improvement and 10 were deteriorated. The children fall into three categories: those with behavior difficulties, the psychopathic and the psychotic. Only 9 of the 50 patients are at present adjusted.

J. A. M. A.

Meninges and Blood Vessels

Torula Histolytica (Cryptococcus Hominis) Meningitis. Stewart H. Jones and Gustavus H. Klinck Jr., Ann. Int. Med. **22**:736 (May) 1945.

Jones and Klinck report their observations on a man aged 50 who had meningitis caused by Torula histolytica.

Despite supportive treatment, which consisted of blood transfusions and the oral and intravenous administration of iodides and sulfadiazine, no improvement occurred. The patient was given gentian violet medicinal intravenously and thymol intramuscularly. No benefit followed the use of either substance. Penicillin was unobtainable in sufficient quantity for adequate therapy. In spite of all efforts, the patient died.

Postmortem examination confirmed the diagnosis of torular infection, which involved the brain, the spinal cord and the kidneys.

In vitro experiments were performed, and sodium sulfadiazine and penicillin showed the greatest growth-inhibiting power. The experiments failed to show any therapeutic value of sodium sulfadiazine in experimental infections in mice.

GUTTMAN, Philadelphia.

DIAGNOSIS AND MANAGEMENT OF SEVERE INFECTIONS IN INFANTS AND CHILDREN: REVIEW OF EXPERIENCES SINCE INTRODUCTION OF SULFONAMIDE THERAPY; IV. PNEUMOCOCCUS MENINGITIS. A. F. HARTMANN, FRANCES M. LOVE, DOROTHY WOLFF and BARBARA S. KENDALL, J. Pediat. **27**:115 (Aug.) 1945.

Hartmann and his associates review the clinical, laboratory and postmortem studies of all patients with pneumococcic meningitis admitted to the St. Louis Children's Hospital from the time the first sulfonamide drug was available for treatment (December 1936) to Nov. 1, 1944. The following conclusions have been reached: Apparently, any type of pneumococcus may cause meningitis. The pathway by which the pneumococcus may gain entrance to the meninges and spinal fluid varies and should, whenever possible, be established because of its possible surgical implications. The incidence of "surgical" mastoiditis as a portal of entry is much greater than with meningococcic infections, but also apparently much smaller than with hemolytic streptococcus infections. When the temporal bone is involved, there seems to be a characteristic pathologic picture which includes (1) a high incidence of purulent labyrinthitis; (2) the formation of "empyemic membrane"; (3) peculiar organization of bubbly exudate, which leads to pseudogland formation, and (4) a high incidence of bilateral involvement. A diagnosis of pneumococcic meningitis can be made with certainty only by lumbar puncture and proper examination of the spinal fluid. The great value of early diagnosis far outweighs any theoretic danger imposed by lumbar puncture. Treatment should be started as early as possible with penicillin and a sulfonamide drug in high dosage. Mortality seems more related to delayed diagnosis and institution of intensive therapy than to any other single factor. Sequelae, such as hydrocephalus, epilepsy and mental retardation, may be expected, especially when the infection occurs during infancy and is not eradicated immediately.

J. A. M. A.

MIDDLE MENINGEAL HEMORRHAGE. R. ORGIAS, New Zealand M. J. **44**:242 (Oct.) 1945.

Orgias describes 7 cases of middle meningeal hemorrhage which were encountered among 1,529 cases of head injury. Of the 67 deaths from head injury, 3 were due to middle meningeal hemorrhage. A detailed inquiry into the circumstances of the accident and the condition of the patient are of great importance for a correct diagnosis. The most useful sign in these cases was coma or a deepening coma or a drift into unconsciousness. The pupil was dilated or had become dilated on the affected side in all cases. The reaction to light was variable, being usually depressed or absent. The pulse was full, and the rate was between 50 and 60. The blood pressure was moderately elevated. There was usually some increase in tone of the limbs or loss of movement on the contralateral side. An inspection of the head with palpation is important, as this may reveal bruising or edema on the side of the lesion. There is usually a fracture across the line of the middle meningeal artery. In certain instances without a history of injury the diagnosis can only be suspected and an exploratory trephine is necessary. Operation should not be delayed. None of the patients showed a dramatic return of consciousness. Therefore efforts had to be directed toward preventing pulmonary complications and maintaining nutrition. The foot of the bed was raised and the patient nursed on the side and rolled to the opposite side hourly. A special nurse kept the airway clear with suction. Three pints (1.5 liters) of nutrient fluid containing 1,500 calories was given by stomach tube daily. The hemoglobin was restored to normal

as soon as possible by blood transfusion to insure adequate oxygenation of the brain. Sulfadiazine, 4 Gm. daily given by stomach tube, helped to control pulmonary infection. All patients were given ½ grain (32 mg.) of phenobarbital twice daily for several months in the hope that traumatic epilepsy could be avoided.

J. A. M. A.

TUBERCULOUS MENINGITIS IN INFANT VACCINATED WITH BCG VACCINE. R. GORLERO BACIGALUPI, Arch. de pediat. d. Uruguay **16**:545 (Sept.) 1945.

Gorlero Bacigalupi reports that an infant who had received BCG vaccine within the first three days after birth, and whose parents and family were normal, developed normally up to 22 months of age, when he became ill with acute tuberculous meningitis and died three days later. The diagnosis was confirmed by cultures of the cerebrospinal fluid and by inoculation of the cerebrospinal fluid into guinea pigs. There was a history of contact of the infant with a tuberculous neighbor when he was 8 months old.

J. A. M. A.

Diseases of the Brain

SUBACUTE BACTERIAL ENDOCARDITIS WITH CEREBRAL EMBOLISM SUCCESSFULLY TREATED WITH PENICILLIN AND HEPARIN. E. T. GREEN, Canad. M. A. J. **53**:425 (Nov.) 1945.

Green reports that after the detection of Streptococcus viridans in three blood cultures, taken on successive days, of a woman aged 25, who first came under observation because of cerebral embolism, penicillin and heparin were given over ten days until a total of 1,200,000 units of penicillin and 200 cc. of heparin had been administered. One week after completion of the course of treatment the patient was sitting out of bed and six days later was allowed to go home. The treatment seems to have had a favorable influence in recovery from the effects of the embolism.

J. A. M. A.

TOXOPLASMIC ENCEPHALITIS. R. S. DOW, Northwest Med. **44**:382 (Dec.) 1945.

Dow presents the histories of 2 patients with toxoplasmic encephalitis. The first was a child aged 2 who exhibited all the clinical manifestations of toxoplasmic encephalitis. These included: (1) healed or inactive chorioretinitis; (2) reduced vision; (3) strabismus, nystagmus and microphthalmos; (4) intracerebral calcification; (5) convulsive seizure (1); (6) internal hydrocephalus from a block at the aqueduct of Sylvius; (7) retarded speech development, and (8) mental deficiency. The case was complicated by the presence of postoperative meningitis and wound infection due to Staphylococcus aureus. The serologic tests for Toxoplasma had not been done, and attempts to infect laboratory animals with spinal fluid were unsuccessful. The second patient, a girl aged 5, exhibited many of the signs and symptoms of toxoplasmic encephalitis. Treatment with sulfapyridine was tried and continued for ten days, a blood level of 5 to 10 mg. per hundred cubic centimeters being maintained. She seemed much improved for three weeks; then seizures recurred. This observation and the results obtained in laboratory animals make it desirable to continue the use of sulfonamide compounds whenever a diagnosis of toxoplasmic encephalitis is made and when there has not been extensive permanent cerebral damage. It is felt that the condition is more common than the reported cases would indicate and that a greater incidence will be found when knowledge of this disorder has become more generally available.

J. A. M. A.

BLAST INJURY OF BRAIN. L. ROGERS, M. J. Australia **2**:209 (Aug. 18) 1945.

Rogers states that structural changes may be produced in the brain or cord of those in the vicinity of an explosion. He reports that a seaman aged 19, after

standing close to a 4 inch (10 mm.) gun during its discharge, noticed a sudden numbness in the left hand and arm, which lasted about ten minutes. Three weeks later began the first of a series of attacks of numbness and tingling, which, starting in the left hand, spread to the elbow, shoulder and side of the face and were accompanied by involuntary abduction and elevation of the arm, spasm of the face and loss of consciousness for a few minutes. On recovery there was some residual weakness of the left upper extremity, which gradually increased and spread to the leg, and seizures became more frequent, occurring four to six times a day. It was decided to explore the postcentral areas, and a bone flap was turned down in this region. The dura in the posterior part of the field was bulging, and when it was opened the cerebral gyri here were seen to be green, widened and elevated over an area about the size of a penny. Incision of the brain in this area revealed a shallow but extensive cavity containing old blood clot. This was removed, and the patient made an uninterrupted recovery; some residual weakness and astereognosis remained. Somewhat similar cases were reported by Mott in World War I, the lesions being discovered at necropsy. It has been suggested that the mechanism responsible for the production of the cerebral lesions is the hydraulic-like pressure transmitted to the cerebrospinal axis in its closed bony walls by sudden compression of the thoracic cage. Such compression must produce violent back pressure on the venous side of the circulation. A sudden rupture of vessel walls may conceivably be caused by the decompression which suddenly succeeds the compression wave.

J. A. M. A.

IMPORTANCE AND VALUE OF ELECTROENCEPHALOGRAPHY IN CRANIOCEREBRAL INJURIES. PUECH, FISCHGOLD, VERDEAUX and BRUN, Presse méd. **53**:547 (Oct. 13) 1945.

According to Puech and his co-workers, a patient with a recent injury and with normal electroencephalograms, or with a slight deviation from normal, will, as a rule, recover rapidly and without surgical intervention provided the alpha rhythm is preserved. A patient with an old injury and with abnormal electroencephalographic tracings after coma has subsided presents a serious problem. Deviation from normal may be caused by hematoma, cerebral edema or hypotension. A recent fracture of the cranium, with concussion and laceration of the brain, may cause slight deviation from normal. The electroencephalographic studies should be made as soon as possible after injury and should be repeated as often as possible, waves from various cerebral areas being recorded simultaneously. Thus, the tracings can aid in ascertaining an improvement in the primary lesion and clarify the situation without resort to operation. In children an injury will cause more deviation from normal than a lesion of the same degree in adults. Considerable deviations at the level of the frontal lobes should not be regarded too seriously. Preventive treatment for epilepsy with sedatives is indicated in cases in which definite deviation from normal continues for a prolonged period after injury. Electroencephalograms and the clinical course were followed for one to ten years after craniocerebral trauma in 15 cases. The tracings showed abnormalities in 9 cases but were normal in the remaining 6. Electroencephalograms can reveal the existence of severe trauma in the past and of a persisting cerebral lesion, but the occasional absence of electroencephalographic abnormality does not exclude the existence of a cerebral lesion.

J. A. M. A.

CEREBRAL METASTASES OF OVARIAN STRUMA. L. DE BAKAY JR. and T. DE LEHOCZKY, Confinia neurol. **6**:22, 1944.

Cerebral metastases of ovarian struma in a woman aged 57 were observed by de Bakay and de Lehoczky. A dermoid containing thyroid tissue was removed from the ovary of the patient. Six to eight years after this operation there appeared indistinct symptoms, such as fatigue and a slight disturbance in gait; later, hyperthyreosis and signs of a supratentorial neoplasm appeared. Mental disturbances

appeared at the same time. Gradually developing left hemiparesis and bilateral papilledema with punctiform hemorrhages were observed, in the absence of sensory disturbance. These symptoms suggested a frontoparietal tumor on the right side. When ventriculographic study was attempted, two incisions in the occipital region revealed a small neoplasm, in the occipital bone. It consisted of thyroid tissue and was considered a metastasis of the previous ovarian struma. This concept was supported by the identical microscopic structure of the ovarian struma and the bone tumor. The case differed from instances presenting the usual syndrome of metastatic brain tumor in that bilateral symptoms referable to the pyramidal tract and impairment of consciousness were observed as late as two weeks prior to death. It is probable that there was another tumor in the right frontoparietal region, a metastasis similar to that in the occipital bone.

J. A. M. A.

CEREBRAL COMPLICATIONS OF RENAL DISEASES IN CHILDREN. C. PAVEZ, Rev. chilena de pediat. **16**:1082 (Nov.) 1945.

According to Pavez, the most important neurologic symptoms of progressive chronic nephritis with hypertension in children are those indicating intracranial hypertension (acute headache, acute meningeal symptoms and either visual disorders or amaurosis). The neurologic symptoms subside with the improvement of the renal lesion, if the latter responds favorably to proper therapy. The differential diagnosis between nephritis and meningitis or cerebral tumor is of importance. The prognosis depends on the course of the renal disease. Two cases of children aged 10 and 13 years, respectively, are reported.

J. A. M. A.

TREATMENT OF BILATERAL ACOUSTIC TUMORS: REPORT OF SIX SURGICAL CASES, WITH REVIEW OF THIRTEEN CASES FROM LITERATURE. R. FRYKHOLM, Acta chir. Scandinav. **92**:451 (Oct. 5) 1945.

Frykholm reports 6 cases of bilateral acoustic tumors in 3 men and 3 women, 5 of them between the ages of 20 to 28 and the sixth a woman aged 44. All the patients received surgical treatment; 1 of them died during the operation, and 2 others showed no improvement and survived only one to two months. The 3 remaining patients were relieved from most of their distressing subjective symptoms and showed improvement in their work capacity. One of them has survived the bilateral intracapsular enucleation of the tumors for more than seventeen years. In the 2 patients on whom surgical intervention was carried out early, the treatment resulted in definite benefit. Cases of general neurofibromatosis in which the lesions are widely distributed within the central and peripheral nervous systems, with the severe alterations not due to the acoustic tumors, should be excluded from surgical treatment. In all cases a bilateral exposure of the cerebellum should be performed. The dura should not be sutured when the wound is closed unless both tumors have been radically removed. If some hearing function is preserved, the tumor on the side on which loss of hearing is most advanced should be attacked first and removed as radically as possible, preferably with preservation of the facial nerve. The patient will probably not improve completely, but he will certainly be in a better condition than if he were totally deaf. The other tumor is not attacked until the general condition begins to deteriorate or loss of hearing is complete. If improvement is not attained by the unilateral extirpation and if the patient's condition is desperate, the other tumor may be extirpated in a second session without regard to hearing function but with care to avoid bilateral facial paralysis. If the patient is already completely deaf, both tumors should be removed as radically as possible. This can be performed in one or two stages, depending on how well the operation is tolerated. If the facial nerve has been preserved during the removal of one tumor, a radical extirpation may be attempted on the opposite side; otherwise only an intracapsular enucleation is performed.

J. A. M. A.

Peripheral and Cranial Nerves

CAUSALGIA SECONDARY TO INJURY OF MAJOR PERIPHERAL NERVES: TREATMENT BY SYMPATHECTOMY. F. F. ALLBRITTEN JR. and G. L. MALTBY, Surgery **19**:407 (March) 1946.

Patients suffering from causalgia continue to be admitted to hospitals with a diagnosis of severe psychoneurosis, and prolonged delay in treatment is a usual occurrence. During this period of delay the changes of disuse affect the extremity. This is of particularly serious import when the hand is involved. Despite the lack of an adequate etiologic explanation of the pain, interruption of the sympathetic nerve supply to the extremity greatly modifies or abolishes the symptoms of the disease. During the twelve months preceding this report, 67 patients were admitted to the hospital with which the authors are associated with injury to a major peripheral nerve and causalgia of sufficient severity to warrant treatment. The seat of the maximum pain was in the distribution of the posterior tibial nerve or of the median nerve. Thirty of this group desired sympathectomy after experiencing relief from sympathetic block. Of this group, 22 had lumbar sympathectomies and 8 had section of the dorsal preganglionic fibers. Good to excellent results were obtained in 28 of the patients. Sympathectomy failed to relieve symptoms and reestablish use of the affected part in 2 patients. The sympathectomy should be of sufficient extent to include the area of injury as well as the area of symptoms. Early sympathectomy will in the vast majority of cases relieve the symptoms of the disease and prevent the profound disabilities of disuse.

J. A. M. A.

CONGENITAL MALFORMATIONS OF FIRST THORACIC RIB: CAUSE OF BRACHIAL NEURALGIA WHICH SIMULATES CERVICAL RIB SYNDROME. J. C. WHITE, M. H. POPPEL and R. ADAMS, Surg., Gynec. & Obst. **81**:643 (Dec.) 1945.

White and his associates report 10 new cases of congenital abnormality of the first thoracic rib. In 5 of these cases operation has been performed for relief of specific complaints, while in 5 others the condition has remained wholly asymptomatic. Malformations of the first rib generally consist of a rudimentary structure terminating in a synostosis or pseudoarthrosis with the second rib near the scalene tubercle or in a free end in the soft tissues at the base of the neck, which may be connected by a ligamentous band with the manubrium sterni. On rare occasions the first rib may have a joint near its lateral angle before it fuses with the second rib. Other skeletal abnormalities which are frequently present and which cause distortion of the thoracic outlet consist in deformities of the second rib and of the upper end of the sternum, scoliosis of the cervicothoracic portion of the spine and vertebral anomalies. Symptoms and clinical evidence of an abnormal first rib consist in supraclavicular bony prominence, irritation or paralysis of the brachial plexus and compression of the subclavian vessels as they cross the defective rib. Cervical arthritis, early carcinoma of the thoracic apex and herniation of a lower cervical intervertebral disk must be considered in the differential diagnosis of brachial neuralgia, even in the presence of an anomalous rib. Malformation of the first thoracic rib cannot be differentiated clinically from cervical rib. It can be accurately diagnosed in an anteroposterior roentgenogram which includes all the cervical and the uppermost thoracic vertebrae, provided the picture is taken with a long exposure and the mandible in motion. A considerable proportion of deformities of the first rib are large enough to cause mechanical compression of the nerves and vessels at the thoracic outlet. When symptoms are attributable to this condition, conservative orthopedic measures should be tried before surgical intervention. Scalenotomy alone rarely suffices to decompress these structures but must usually be accompanied by radical resection of the rib from a point close to its articulation with the transverse process forward to its attachment to the second rib or where it disappears beneath the clavicle.

J. A. M. A.

DENERVATION AND RE-INNERVATION OF HUMAN VOLUNTARY MUSCLE. R. E. M. BOWDEN and E. GUTTMAN, Brain **67**:273, 1944.

Bowden and Guttman made biopsies of 140 specimens of muscle from 86 cases of peripheral nerve injuries and studied the innervation, denervation and reinnervation of human muscle in this material. Denervation produces progressive and ultimate shrinkage of the muscle fibers. Up to three years after denervation no degeneration or disruption of muscle fibers is observed, but shrinkage of fibers and increase of connective tissue may be so advanced that reinnervation does not produce a well functioning unit. The essential changes during this three year period are progressive, but unequal, shrinkage of muscle fibers, progressive depletion of the sarcoplasm of the end plate, progressive distortion of the pattern of innervation and vascularization. After this interval disruptive changes occur, and longitudinal splitting of muscle fibers together with shrinkage takes place. Fragments of myofibrils become embedded in connective tissue, and in the latest stages muscle fibers may be represented by tubes filled with pyknotic nuclei and granules or fragments of muscle tissue. The pattern of innervation is intact for three months after denervation. After this the end plates become increasingly difficult to identify, and the pattern of innervation is distorted by the proliferating connective tissue. Permeability of the vessels is increased soon after denervation. The walls of the vessels then become thickened and the capillary bed is reduced. In the latest stages of denervation muscle is represented by fat, connective tissue, vessels and the larger empty nerve trunks. Within three years the changes in the muscle may be reversed to some extent by reinnervation. After three years it is questionable whether useful recovery is possible.

Bowden and Guttman conclude that biopsy of muscle is a useful aid in the diagnosis, prognosis and treatment of peripheral nerve injuries. Biopsy observations must be evaluated with respect to the state of the muscle and the nerve and the period of reinnervation. Different types of lesions of the nerve trunk produce characteristic patterns of reinnervation, and thus it is possible to differentiate neurotmesis, axonotmesis, partial lesions and such entities as traction injuries, unaided unions and unsuccessful sutures.. After axonotmesis the rate of growth of axon tips is probably not greater than 3 mm. per day. Biopsy observations must be considered in connection with full clinical data. The limitations of the biopsy method are as follows: (1) The biopsy specimen may contain no nerve fibers; (2) the smallness of the specimen may involve error, and (3) the necessary period of waiting for reinnervation before biopsy may not be justified.

FORSTER, Philadelphia.

TRAUMATIC INJURIES OF PERIPHERAL NERVES: I. SIMPLE COMPRESSION INJURIES OF THE RADIAL NERVE. SYDNEY SUNDERLAND, Brain **68**:56, 1945.

In order to determine the course of regeneration in cases of simple compression lesions of the radial nerve, Sunderland observed 7 patients, 5 of whom presented compression of the nerve in sleep, 1 had compression due to faulty use of crutches and 1 had been pinned beneath a truck. Restoration of function was determined by return of full range and power of movements. Wasting of muscles was determined by measurements of the arms at fixed points. Some variation in the degree of motor involvement was present. Sunderland observed that electrical excitability and sensation were not impaired to the same extent as was motor power. The escape of sensory fibers from the compression is attributed to a combination of factors, including anatomic arrangement of fibers, differential susceptibility of different types of fibers and perhaps other biochemical or morphologic properties. Sensory defects appear with the more severe injuries and indicate that restoration of motor function will be delayed. Muscular wasting occurred in 5 of the 7 cases. This is assumed to be due to early and rapid restoration of function. A normal nerve may be involved during sleep if the compression is sufficiently severe and prolonged. In all instances recovery was spontaneous and

in 5 cases occurred three to four months after injury. The course of recovery in cases of nerve compression differs from that in cases of nerve division and resuture in the following ways: (1) Spontaneous reappearance of function following compression occurs in from fifteen to more than sixty-one days; (2) recovery appears simultaneously in muscles in which lengths of the nerve fiber vary; (3) there is no orderly progress of regeneration; (4) two or more muscles may begin simultaneously to contract again, and once conduction reappears in one muscle a short interval elapses before all muscles supplied by the nerve are contracting; (5) the site of the first appearance of recovery varies, and more distally supplied muscles may recover first; (6) the time of appearance of motor function and the time required to recover power completely in the various muscles are in no way related to the length of the nerve fibers.

Sunderland concludes from these observations that the histopathologic changes leading to interruption of conduction after simple compression injuries differ from those occurring after anatomic interruption of the nerve fibers and that these changes are reversible and do not involve wallerian degeneration.

FORSTER, Philadelphia.

LESIONS OF THE NERVOUS SYSTEM ASSOCIATED WITH POLYRADICULONEURITIS. D. NIETO, Bol. lab. de estud. med. y biol. **1**:261 (Dec.) 1942.

Nieto reports anatomic studies in 2 cases of polyradiculoneuritis. A man aged 42 was admitted to a hospital for mental disease with a clinical picture of an exogenous psychosis, probably alcoholic. The period of confusion cleared up after eleven days at the hospital. Two weeks later polyneuritis began to develop. There were pronounced motor changes and less severe impairment of sensation. The patient died of pneumonia two months after the onset of the polyneuritis. There was no fever during the course of the disease. The spinal fluid showed 11 cells per cubic millimeter, with 200 mg. of albumin per hundred cubic centimeters. In the second case the clinical diagnosis was poliomyelitis. Histologic examination in this case showed a condition very similar to the first. The author believes that he is justified in considering that these patients had the same disease.

Macroscopic examination of the spinal cord and spinal meninges showed nothing significant. Microscopic examination of the spinal cord showed diffuse lesions in the anterior horns, which were evidently secondary to involvement of the roots and peripheral nerves. The histologic picture was that of retrograde degeneration. There was no evidence of perivascular infiltration within the cord and no cellular response in the meninges. There was no increase in microglia cells; a mild reaction of the oligodendroglia was noted.

The roots and nerve trunks were slightly swollen. Microscopic examination of the roots and peripheral nerves showed some congestion, with dilated vessels; rare small hemorrhages, and occasional perivascular infiltration. There was pronounced degeneration of the axis-cylinders and myelin sheaths.

The author doubts whether an inflammatory process could have been the cause of such extensive changes in the roots and nerve trunks without some meningeal infiltration. He thinks that the inflammatory reaction within the peripheral nerves and roots was probably secondary to degeneration of the nerves. As a result of his histologic observations in these 2 cases, he is inclined to believe that the pathologic process was due to action on the nerves of a toxic agent.

N. SAVITSKY, New York.

NEUROGRAPHIA. A. ASENJO, M. CONTRERAS and C. VILLAVICENCIO, Rev. de psiquiat. **10**:54, 1945.

The authors report 2 cases in which the precise site of injury to peripheral nerves was demonstrated by the injection of iodized poppyseed oil into and around

the nerve. Saito, in 1933, suggested the intraneural and perineural injection of a colloidal suspension of thorium dioxide. The authors used iodized poppyseed oil because the thorium dioxide caused rather pronounced connective tissue reactions. The amount of iodized oil injected varied with the thickness of the nerve (from 0.5 to 2 cc.). About one-fourth the amount was injected into the perineural region and the rest into the nerve itself. No harmful effects from the injection of iodized poppyseed oil were observed in either case. Operation in both cases confirmed the existence of lesions at the site of abnormality of the nerve after injection of the oil.

N. SAVITSKY, New York.

Treatment, Neurosurgery

COMPOUND, COMMINUTED SKULL FRACTURES PRODUCED BY MISSILES. E. H. CAMPBELL JR., Ann. Surg. **122**:375 (Sept.) 1945.

Summarizing his observations on 100 cases of compound, comminuted fractures of the skull, Campbell says that inner table fractures were sometimes overlooked and occasionally led to serious complications. Tripod incisions often gave trouble; it is recommended that they be avoided when possible. Convulsions were uncommon in the first few weeks; their occurrence was sometimes an early manifestation of abscess formation. Subdural hematoma was present in but 2 cases. Superficial wound infections of varying degrees developed in 19 cases, while in 22 the infections were deep seated. These were manifested by abscess, meningitis or cerebral fungus. There were 5 deaths, all of which occurred in the latter group. Incomplete débridement was the largest single factor contributing to wound infection. In those cases in which all bone fragments had been removed infection was uncommon and seldom deep, whereas if débridement had been incomplete or not performed infection was common and usually deep. Bacteria cultured from these wounds were principally skin inhabitants of low virulence. Treatment consisted in evacuation of pus and removal of associated bone fragments and/or metallic foreign bodies as well as of adjacent necrotic tissue and old blood. Abscess capsules were disturbed as little as possible. Sulfonamide therapy was employed as an adjuvant. Failures resulted only in those 5 cases in which, for one reason or another, this procedure was not carried out. Experience, judgment and skill, as well as the proper neurosurgical armamentarium, are prerequisite to good primary débridement.

J. A. M. A.

REHABILITATION OF PATIENTS TOTALLY PARALYZED BELOW THE WAIST, WITH SPECIAL REFERENCE TO MAKING THEM AMBULATORY AND CAPABLE OF EARNING THEIR LIVING: I. ANTERIOR RHIZOTOMY FOR SPASTIC PARAPLEGIA. D. MUNRO, New England J. Med. **233**:453 (Oct. 18) 1945.

Munro asserts that a patient with an injury to the spinal cord or cauda equina who is intelligent and cooperative and has the use of the shoulder, arm and hand muscles can be made ambulatory, can have such control of the bladder and bowels as to sleep through the night without either getting up or wetting himself, can carry out ordinary activities throughout the day without soiling himself with feces or having to evacuate his bladder oftener than once every three hours, can lead a normal social life and can earn a living. This paper is the first of a series that describes certain therapeutic procedures that have made the attainment of these end results possible. The author has performed a bilateral dorsolumbar anterior rhizotomy on 10 patients. This bilateral intraspinal division of the anterior roots of the eleventh thoracic through the first sacral spinal nerve is recommended as a means of changing a spastic to a flaccid paraplegia in patients with an anatomic transection of the spinal cord at any point between the second thoracic and the second sacral segment preliminary to making the patients ambulant and to providing them with complete twenty-four hour control of micturition, so that they may again become active members of their community and be self supporting.

Because this operation is a permanently destructive one, the indications for performing it should never be considered lightly. For the present, at least, it should be strictly limited to patients in whom the spinal cord is anatomically transected and in whom all neural connections between the cut surfaces of the cord have been destroyed.

J. A. M. A.

PENTOTHAL SODIUM ANESTHESIA IN NEUROLOGIC SURGERY. EDWARD W. SHANNON and W. JAMES GARDNER, New England J. Med. **234**:15 (Jan. 5) 1946.

The study was made on 101 unselected neurosurgical patients who were cared for at the Cleveland Clinic. Pentothal sodium anesthesia was induced in these patients and "in several hundred major neurosurgical procedures." No death could be attributed to the anesthetic.

The technic employed consisted of administration of an enema and 0.1 Gm. of seconal sodium the night before the operation. The meal before the operation was omitted, and 0.1 Gm. of seconal sodium was given two hours before the operation. Forty-five minutes prior to operation adults received 0.65 mg. of atropine sulfate and children a proportionately smaller dose. If the patient was unusually apprehensive, morphine was given with the atropine.

Pentothal sodium was administered in a 2.5 per cent solution via a side arm, which was connected to an apparatus for the intravenous administration of 5 per cent dextrose in isotonic solution of sodium chloride.

In the experience of these authors, pentothal sodium as an anesthetic is "superior to all others for craniotomy." The induction of anesthesia is brief, and the patient is under an anesthetic for a shorter time. The authors state that there is no increased intracranial pressure; hence, bleeding is reduced. Postoperative vomiting and retching are an unusual occurrence following pentothal sodium.

This anesthetic agent was successfully employed in all types of craniotomy and operations on the spinal cord. The authors conclude that induction of anesthesia with intravenous administration of pentothal sodium has been found to be extremely satisfactory and safe for neurologic surgery. GUTTMAN, Philadelphia.

TROPICAL HEADACHE: PRELIMINARY REPORT ON DIAGNOSIS AND TREATMENT. W. W. WOODS and J. W. STUTZMAN, U. S. Nav. M. Bull. **46**:501 (April) 1946.

Woods and Stutzman examined 20 young men suffering from severe, incapacitating headache for which no specific cause could be found. Five patients had severe unilateral frontotemporal headaches; the remaining 15 patients had bilateral frontal headaches. The unilateral type is to be considered as caused by abnormal extracranial vasodilatation. The pain is conducted by afferent fibers coursing along the vessels and may often be relieved by selective arterial resection. The unilateral pain did not respond to therapy consisting of increased intake of salt, calcium and fluids or of injections of neostigmine methylsulfate. It was made worse by heat and exertion and by compression of the jugular vein produced by infection of a blood pressure cuff about the neck to 35 mm. of mercury for three minutes. The second type, represented by the 15 cases of bilateral frontal headache, is to be considered as arising from intracranial vascular structures. In all these cases the headache was made worse by heat and exertion but was often improved by compression of the jugular vein. Occlusion of the carotid artery seemed to relieve the headache on that side only and often made the pain worse on the opposite side. Occlusion of extracranial arteries had no effect. Since the headache was accompanied with decreased intracranial pressure in the upright position, was made worse by lowering the level further and was abolished by raising the pressure, it could be assumed that traction on the intracranial vessels was a factor. This type of headache was definitely relieved by increased intake of salt, calcium and fluids and by injections of neostigmine methylsulfate.

J. A. M. A.

TREATMENT OF HEMOPHILUS INFLUENZAE MENINGITIS WITH SULFONAMIDES IN CONJUNCTION WITH HEMOPHILUS INFLUENZAE, TYPE B, RABBIT ANTISERUM. E. A. NORTH, H. WILSON and G. ANDERSON, M. J. Australia **1**:215 (Feb. 16) 1946.

North and his associates discuss the treatment of children with Hemophilus influenzae meningitis at the Children's Hospital, Melbourne, and the Royal Alexandria Hospital for Children, Sydney. Of 157 children of all ages who did not receive specific treatment, 2 (1.2 per cent) recovered; of 150 who were treated with sulfonamide compounds, 32 (22 per cent) recovered; of 81 who were treated with sulfonamide drugs in conjunction with type B Hemophilus influenzae rabbit antiserum, 46 (56.8 per cent) recovered. Recovery under treatment was more frequent with each year of age. The poorer prognosis for very young children was probably due to delay in the beginning of specific treatment resulting from late diagnosis, in consequence of the difficulty of recognizing meningitis early in such children without resorting to lumbar puncture. It was possibly due also to the absence of natural antibodies in the blood of young children and to their relatively poor immunity to infection. One of the sulfonamide drugs should be given. A bacteriologic diagnosis should be urgently sought, and specific antibody contained in rabbit serum should be injected as soon as the diagnosis is reached.

J. A. M. A.

TREATMENT OF CEREBRAL ABSCESS WITH SULFONAMIDE COMPOUNDS. J. PIQUET, Presse méd. **54**:87 (Feb. 9) 1946.

Piquet reports the results of sulfonamide therapy of 15 patients operated on for cerebral abscess of otitic origin. Nine had a cerebral abscess and 6 a cerebellar abscess. Six patients with cerebral abscess and 2 with cerebellar abscess recovered. Treatment consisted in surgical removal of the initial focus; drainage of the abscess, with an iodoform drain allowed to remain in the cavity, and occasionally of decompression. A dose of 8 to 10 Gm. of the sulfonamide compound was administered daily for one week, and treatment was continued with smaller doses, depending on the improvement. Two patients had recurrence of the abscess. Sulfonamide therapy apparently improves the prognosis of a cerebral abscess by checking the encephalitis in the adjacent area of the abscess, but control of the patient for the next three months is essential because of occasional recurrence. Increased cerebral pressure may be relieved by puncture of the dura in the area of the primary abscess. An iodoform drain should be placed in the cavity for two to three months and be changed every eight to ten days. Neither local nor general sulfonamide therapy was effective in cases of cerebellar abscess. It was demonstrated that the white substance of the brain fixed twice as much of the sulfonamide drug as the cerebellar tissue.

J. A. M. A.

Society Transactions

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Madelaine R. Brown, M.D., Presiding

Regular Meeting, Nov. 29, 1945

Tonic Effect of Insulin in Acute Alcoholism. Dr. Etem G. Vassaf, Boston, and Dr. Volta R. Hall Jr., Arlington, Mass.

A series of 43 patients admitted for treatment of uncomplicated acute alcoholism was presented. In addition to the usual regimen of a high calory, high vitamin diet; forcing of fluids; use of supplementary thiamine hydrochloride, an antacid and a bitters tonic; chloral and bromide sedation; physical therapy; occupational therapy; psychotherapy, and gradual withdrawal of alcohol over a maximum period of three days, these patients were given 10 units of insulin twenty minutes before meals two or three times a day without the administration of dextrose as such. A comparison of patients receiving insulin in this fashion with the controls showed results in favor of the insulin method: (1) The average period of withdrawal was reduced by one-half; (2) only one-third as many patients required or demanded whisky after admission; (3) there was increase in subjective ease and comfort during the period of withdrawal; (4) the amount of supplementary sedation required was markedly decreased, and (5) the average gain in weight, both during the first week of hospitalization and subsequently, was tripled. In spite of the insulin being covered only by the food of the subsequent meal, insulin reactions were rare and were readily controlled with oral administration of orange juice and cane sugar, although dextrose was always at hand for intravenous injection.

The clinical findings were discussed in the light of former laboratory studies on the relation of insulin and of dextrose to the oxidation and detoxification of alcohol and of clinical observations on the use of a combination of insulin and dextrose in treatment of simple acute alcoholism, as well as of the more severe toxic states, such as delirium tremens. It was suggested that the action of insulin may be due not only to its indirect effect in the detoxification of alcohol, via its furtherance of oxidation of dextrose, but also to a direct effect of the insulin itself, as certain previous studies have indicated.

It was pointed out that the addition of small doses of insulin alone to the regimen of treatment of acute alcoholism is of distinct clinical value and that the results compare favorably with those of the combined administration of insulin and dextrose. The treatment is recommended as a valuable addition to the therapy of acute alcoholism.

DISCUSSION

Dr. W. H. Forbes, Brookline, Mass.: I was much interested in this paper, but I am handicapped in discussing it because most of the material is outside the realm of my experience. Such work as I have done along this line has not yet been published. It was started in cooperation with Mr. Norman Riung but was never completed, as he, who was the more active partner, was killed during the war. The studies about which we have just heard were concerned with chronic alcoholism. Those carried by Riung and me dealt only with acute alcoholism. Fasting subjects drank 2 ounces (60 cc.) of whisky (100 proof) mixed with water and then performed a series of psychologic tests. After establishing a curve showing the normal response to this dose, we gave the subjects either dextrose or insulin (or in some experiments we altered the oxygen tension), with striking results, which, however, differed materially from those just presented. Either dextrose or oxygen produced striking improvement in performance, whereas insulin or a

low oxygen tension caused great deterioration. These results are dependent, however, on making the observations within the first two hours after administration of the alcohol. After that period our results were quantitatively very different. The best period in which to show the effects of insulin or dextrose was one-half hour after the ingestion of the alcohol, at which time both its concentration in the blood and its effect on the performance of the subject were at their peak. The injection of 2 units of insulin at this time, a dose which would have a barely perceptible effect on the normal person, caused the subjects who had taken the alcohol almost to pass out. The test we used principally was the Johnson code test, and with the average subject the length of time taken to perform the test was increased by the dose of alcohol by about 25 per cent. For the subjects who had insulin without alcohol the increase was about 10 per cent, but the subjects who had both alcohol and insulin were unable even to write, let alone to do any coding or decoding.

The oxidation of the alcohol during the first hour did not seem to be greatly influenced by either dextrose or insulin. The improvement due to the giving of dextrose and the deterioration due to the injection of insulin were not attributable to the level of alcohol in the blood, as this was the same in the controls and in the two experimental conditions.

I am inclined to think that the picture after an alcoholic bout of considerable duration is quite different from the picture we were studying. This impression is based on observations at the Boston City Hospital in which my associates and I gave dextrose to subjects in the ward for alcoholic patients. Some of the patients who had taken alcohol very recently showed dramatic reduction in the level of intoxication, but the subjects who had been consuming large quantities of alcohol for some time showed negligible effects of the dextrose. We did no experiments with insulin at this hospital.

DR. JOSEPH THIMANN: I gave insulin to 16 acutely intoxicated patients, according to the method of Tillim. The ages of the patients varied from 27 to 61 years. The length of the last drinking spell ranged from three days to nine weeks. For the majority of patients it lasted about one week. The amount of whisky consumed during the last spell varied from 1 pint to 2 quarts (½ to 2 liters). One patient consumed a gallon (3.8 liters) of whisky in three days. Five of the patients were "repeaters," giving me an opportunity to compare the insulin treatment with the conventional method of paraldehyde therapy, supplemented if necessary with dextrose, insulin and vitamins. In 11 of the 16 cases both patient and staff felt that the insulin method was definitely superior. In 4 cases the effect was as good as that of paraldehyde. In 1 case it was our opinion that paraldehyde therapy would have been the method of choice. It might be preferred in the management of severe delirium. The majority of patients recovered from the acute intoxication with fewer side effects than with paraldehyde. For 1 patient, aged 33, it was his second admission. His drinking spells were periodic. His last bout had started one month before. He drank more than a quart (liter) of whisky a day. He had had no solid food for the week preceding admission. On admission he was moderately intoxicated, with unsteady gait. He was fairly cooperative. The pulse was regular with a rate of 100; the blood pressure was 150 systolic and 90 diastolic. Tendon reflexes were absent in the lower extremities and hypoactive in the upper extremities. He received 60 units of insulin intramuscularly at 6:20 p. m. An hour later, he was asleep and his pulse rate was 110; he perspired moderately, and respiration and color were good. Two hours later, when roused, he said he felt well but was hungry and thirsty. Thirty minutes later, two hours after the injection, he was perspiring profusely; the blood pressure was 170 systolic and 110 diastolic. He received orange juice with sucrose. At 1:15 a. m. he could not sleep. He was given 0.2 Gm. of phanodorn. After that he slept until morning. He felt fairly well and was transferred from the ward to a private room. There was no nervousness. It appears that the insulin treatment of this patient was more successful than the conventional method; during his

previous stay at the hospital he was less heavily intoxicated on admission but had to be given 22 cc. of paraldehyde on his first day, 18 cc. on his second day and was unable to leave the admitting ward before the third day, and did not feel well even then.

In addition to these advantages, it is, in my opinion, especially gratifying that insulin therapy enables one to avoid treating the effects of one depressant (alcohol) with another depressant (paraldehyde). The insulin method will also take away the ammunition from those patients who, resenting the sudden withdrawal of alcohol, say sneeringly that paraldehyde is nothing but alcohol mixed with formaldehyde so they might as well taper off with a few drinks. Insulin treatment would also probably obviate addiction to paraldehyde in those "old timers" who make futile attempts to taper off with the help of self-prescribed paraldehyde.

I should like to refer to an article by Lolli and Greenberg, of Yale University (Effect of Insulin on Rate or Disappearance of Alcohol from the Stomach, *Quart. J. Studies on Alcohol* **3**:92 [June] 1942). The authors of this article stated the belief that they had demonstrated that insulin induces more rapid gastric emptying and thus may increase the concentration of alcohol in the blood. In view of the fact that this observation may not be irrelevant in cases in which the alcohol level of the blood is high, bordering on the production of alcoholic coma, I wonder what Dr. Vassaf and Dr. Hall would think of preceding the insulin treatment by an injection of emetine hydrochloride, thus emptying the alcoholic contents of the stomach outward instead of into the blood.

DR. JOHN A. ABBOTT: I believe that you value insulin highly for its sedative effect.

DR. ETEM G. VASSAF: Our purpose in presenting this paper was to show that the method is simple and does not require a high degree of teamwork on the part of nurses and attendants. Patients receiving larger doses of insulin should, of course, get more carbohydrate in order to prevent any secondary reaction. Our findings, however, show that satisfactory results can be obtained with relatively small regular doses of insulin, without the necessity for large supplementary amounts of dextrose. We did, of course, stress an adequate food intake to make up for the poor diet which these patients have usually been receiving. We also noticed that dehydration was frequently an important factor and gave liberal amounts of fruit juices and other fluids. We did not give insulin intravenously because of its rapid, but short, action, which increases the possibility of coma, while lessening the therapeutic effect.

We were particularly impressed with the reduction possible in supplementary sedation. Paraldehyde has been used consistently in high doses in many institutions but is sometimes found to cause respiratory difficulties or to accentuate respiratory complications. Sometimes it has even been used intravenously; this is not good policy. Therefore, the less paraldehyde or other sedative used, the better.

DR. VOLTA R. HALL, Arlington, Mass.: As Dr. Thimann points out, insulin has an effect on gastric motility. But I do not think that the favorable results of insulin in these cases can be explained on that basis, since the effect of insulin obtains even into the second or third week. The use of emetine to empty the stomach of its alcohol promptly is theoretically sound, as in any case of acute poisoning by the oral route. From the practical point of view, however, its use might be limited by many patients being unwilling to present themselves for treatment at all if faced with the certainty of violent nausea and vomiting immediately on admission.

One meets something of the same problem in regard to the question of abrupt withdrawal versus tapering off. Doubtless, the former is the method of choice; but, again, many patients object strenuously to it. That we were able to accomplish immediate withdrawal in almost half our patients, without putting any pressure on them, or causing any hard feelings, is, we feel, worth while.

With regard to Dr. Forbes's observations, alcohol taken over a considerable period impairs glucose metabolism, and there is evidence that a certain amount

of glucose is present which cannot be utilized. In the cases described by Dr. Forbes, as he points out, the setting was somewhat different, but the results must be included in one's total thinking on the subject.

Incidentally, we had vaguely hoped that we might see a lowering in the rate of readmission. However, we cannot say that insulin makes any difference in the patient's psyche or in his propensity for intake of alcohol.

Syndrome of Cerebral Concussion from Air Blast. COMMANDER ROBERT S. SCHWAB (MC), U.S.N.R.

In World War I the syndrome of shell shock was given considerable prominence in the medical literature. The symptoms of the condition identified with this diagnosis were supposed to have been produced by the effect of blast from nearby exploding shells on the human brain. It was thought that the force of the blast transmitted through the air and into the cranial cavity destroyed the cytoarchitecture of the cortex by a sort of molecular disruption and that this cerebral damage produced the clinical signs that were associated with the condition. These were extreme irritability, strong startle reaction, bizarre tremors and automatic movements, some loss of memory, headaches and a striking decrease in efficiency. The absence of neurologic signs with these symptoms and the lack of other data that would indicate structural damage to the brain caused many investigators at the time to doubt whether these effects were due to the physical energy of the blast. The production of identical symptoms by factors other than nearby explosions, such as the violent, disruptive death of a companion or some other horrible emotional experience, as well as the successful treatment of many of the victims with purely psychiatric procedures, finally reduced shell shock to the category of a severe hysteria-anxiety syndrome and the term "shell shock" fell into disrepute.

In the recent war, as a result of the intensive bombing and greater destructive power and size of the explosives used, the term "blast concussion" appeared in the medical literature in 1940. It was supposed, as in the first world war, that these gigantic bomb blasts would result in direct damage to the brain. Various articles have been published on this syndrome, and it is an accepted diagnostic term in both the Army and the Navy.

The present report deals with clinical observations on about 350 patients seen in the Pacific theater in 1944-1945 who were admitted to naval hospitals with a diagnosis of "concussion, atmospheric, cerebral."

The first large group of patients who were observed were in a naval hospital in the Hawaiian Islands, to which over 100 men given this diagnosis were admitted. The second group consisted of 105 patients from Iwo Jima, and the third group, of 150 patients received during the Okinawa campaign; both groups were seen at Guam. A smaller group, of about 25 men from the Bougainville campaign, were examined in a hospital in New Hebrides. I saw about a dozen patients given this diagnosis at the Chelsea Naval Hospital in 1943; these men had received their initial blast effect the previous year on Guadalcanal.

Since all these patients had been exposed to the near blast of either bomb or shell explosions, it might be well at this point to describe the general effect of an air blast in the open and to relate personal observations on it.

I had an opportunity for temporary duty on a heavy cruiser which was engaged in battle practice involving considerable use of 8 inch (20 cm.) guns. Since this was not an actual battle condition, it was possible to be stationed on the wing of the bridge, about 20 feet (6 meters) from the 8 inch gun, during broadside fire. Knowing the damage to the ear drums from such proximity to these discharges, I insured against such injury by careful application of cotton in the auditory canals. The primary objective was to note the effect of pure blast and to determine whether it would produce headache or other uncomfortable sequelae. There was no danger, of course, in such a position of being injured by any fragments. For the better part of a day and one evening I stood by these guns to observe the effect of the blasts. In spite of the cotton in the ears, the blasts were exceed-

ingly unpleasant to the ears. The force of the air wave would push one about and tear one's shirt. A pair of spectacles was blown off in one of these blasts. The incandescent yellow flash, when observed directly in the daytime, rendered the eye blind for thirty to forty seconds. When observed once during the night, with the pupil dilated, temporary blindness lasted about four and a half minutes. No headache or other somatic disturbance was noted. The intensity of the blast effect was calculated by an ordnance expert as being about the same as that of a 100 pound bomb or shell exploding at the same distance.

As a result of this observation, it seemed unreasonable that the effect of pure blast would injure the brain in the cases observed. The nature of the blast wave is such that in the open atmosphere the compression effect is rapidly dissipated, so that a few yards away from the exploding missile the crushing effect of the air pressure has diminished to a degree that it could not damage a structure like the cranium. However, if it were intense enough, the compressing effect could very well crush soft organs containing air or fluids. One would suppose therefore that if the brain were damaged by such an effect there must always be extensive damage to the lungs, viscera, blood vessels, eyeball and sinuses. The ear drums, which respond to such pressure readily, would always be ruptured under such conditions. Now this is not the case. In 90 per cent of the patients seen the ear drums were intact. In all but 3 of the patients observed there was no evidence of blast effect in the organs aforementioned. Furthermore, in the 3 exceptions noted the blast did not occur in the open but took place in a confining space, where the effect of pressure could not be dissipated and where, therefore, the blast might be expected to produce compression effects on the brain. Neurologic examinations of these 3 patients revealed definitely abnormal signs. On the other hand, for well over 300 patients bearing this diagnosis the results of neurologic examination were within normal limits—clinical evidence that there was no cerebral damage. In a small group, i. e., 15 men, the spinal fluid was under normal pressure and free from red blood cells and increase in protein. In a larger series, i. e., 75 men, not seen by me, but reported on verbally by Lieutenant Commander Fogel, of the U. S. S. *Bountiful,* the spinal fluid was normal in all.

About 40 per cent of these patients complained of a definite period of amnesia, lasting anywhere from thirty minutes to thirty hours. It is this amnesia which has led many clinicians to the conclusion that cerebral damage must be present. Analysis of the amnesia in this group of patients reveals the following characteristics: None showed any retrograde amnesia. Retrograde amnesia is usually found in cases of damage to the brain from injury to the skull. In fact, the amnesia usually reported in this series began after the subject had heard the explosion and felt himself pushed down by its effect. In all cases in which the amnesia was explored by means of narcosynthesis (pentothal) or hypnosis restoration of memory was possible. This is not considered characteristic of the amnesia associated with cerebral damage. In many cases the amnesic material revealed a serious panic state with complete loss of control: violent fear reactions and surrender to the flight impulse. Of course, in well trained fighting men such behavior produces an intense feeling of guilt and shame, so intense that unconscious burial by means of amnesia is the only way out. In a number of cases exploration of the amnesia revealed a period of recall which ended shortly after an injection of morphine or a barbiturate. This medication, then, produced a "natural" sleep, which could not be further explored and which certainly could not be explained by any means as a result of damage to the brain but, rather, was only the normal effect of strong sedation. Illustrative cases will now be described.

Case 1.—A pharmacist's mate aged 19 was brought into the hospital by air with a diagnosis of air blast concussion, which had occurred twelve hours before on Okinawa. He had been in the front lines administering to the wounded for six days. He was suffering from deprivation of sleep, inadequate food and water intake and extreme fatigue. He had been under heavy artillery and mortar fire most of the time. His past history was free from neurotic illness or breakdown. The last thing he remembered was a shell exploding near him, and he woke up

in the evacuation airplane four hours later. Neurologic examination revealed nothing pathologic. There were a strong startle reaction, extreme anxiety, tremor of both hands and tremulous speech. Under pentothal narcosis he relived his battle experience readily, a summary of which follows: A mortar blast nearby pushed him on top of a patient to whom he was trying to administer plasma and spoiled the procedure. He began to shake violently at the time. He dragged his patient into a foxhole but was unable to give him any more first aid. The patient, he believed, was dead by that time. A sense of failure overwhelmed him. At that time he heard a terrific explosion above the foxhole, and then the period of amnesia began. During the pentothal narcosis he remembered crawling out of the foxhole, screaming and crying, and trying to get up on his feet and run toward the aid station. He passed two other wounded, or possibly dead, Marines during this struggle. Another corpsman aided him, put him into a tank or tractor and took him to the dressing station. He recalled being given some sedation and being wrapped in a blanket and put into an ambulance. He remembered crying and sobbing during the entire ambulance trip to the airfield. The intense guilt of this man's breakdown, occurring at a time when he was thoroughly exhausted, would cover the mechanism of the amnesia. There was no evidence whatever of damage to his brain; recovery took place in three weeks, and he was returned to duty.

CASE 2.—A Marine sergeant, after twelve days in the front lines at Iwo Jima under conditions of extremely heavy fighting, was in a trench when a large bomb or torpedo exploded nearby. He remembered being covered with black dust and hearing the noise of the explosion. He had amnesia for sixteen hours after this. Under pentothal narcosis, he recalled readily that he stayed in the foxhole, afraid to move, with the dust in his nose and mouth. He was picked up by a stretcher group and taken back to the beach, which was also under fire. On the landing vessel, which was taking him to the ship, he opened his eyes to witness the futile efforts of two corpsmen to save a man dying of a horrible wound of the throat, in spite of a physician's attempt to get in a tracheotomy tube. The retelling of this part of the episode brought out tremendous agitation, anxiety and hyperventilation. The patient improved greatly after the clearing of his amnesia with rest and sedation and probably was able to go back to noncombat duty after he left the hospital. There was certainly no evidence of an organic lesion of the brain in this case.

CASE 3.—A medical officer during an aerial bombardment was walking down the corridor of a landing ship tank, when a 200 pound bomb exploded in the adjoining passage, spraying an area with fragments 2 feet (60 cm.) in front of him. He was knocked down and was unconscious for a few minutes. He had no recollection of the blast or of the fragments hitting the wall in front of him. The last thing he remembered was leaving his cabin to go to his battle station. He showed bilaterally ruptured ear drums; loss of hearing, which was partially permanent; bleeding from the nose; moderate bleeding from the lungs; some bleeding from the intestinal tract; bilateral retinal hemorrhages, which cleared up, and definite weakness of the left leg, with a Babinski sign. He did not have the startle reaction, tremor and anxiety or other symptoms described in the preceding cases. There was an undisclosed number of red blood cells in the spinal fluid. All these signs disappeared except the loss of hearing, and he was able to return to duty three months later. This is 1 of the 3 cases in which a true air blast concussion was encountered and occurred in a confined space, where air pressure could be built up.

CASE 4.—A soldier, running across an open space between two hills in the front line, was thrown by a blast from a small mortar shell against a tree, striking his helmet so violently as to produce a large dent in it on the left side. He was dizzy for a minute and had a sharp tingling in his right foot. He did not lose consciousness. When admitted to the hospital, he had a large hematoma of the scalp; weakness of the right leg, which disappeared in two hours or so, and persistent left-sided headaches, which kept him on the sick list for some time

and eventually caused his evacuation to the United States. This man undoubtedly had a cerebral injury which was produced by his crashing into the tree, and not a blast concussion at all.

In conclusion, it is felt that in the vast majority of the so-called cases of air blast concussion—over 90 per cent—the condition is an extreme hysteroanxiety state produced in men who have been exhausted or otherwise conditioned to this form of trauma. There is no evidence in my observations of damage to the brain or the nervous system. A diagnosis of air blast concussion in these cases places the men in a surgical category that is not justified by the facts and deprives them of important prompt psychotherapy. It is regretted that no facilities for electroencephalographic recordings were available in this study.

DISCUSSION

DR. WILLIAM H. SWEET: I am much interested in Commander Schwab's account, for during a period of three and a half years of living in a British city (during the entire time that the United States was in the war), in which I was doing the neurosurgical work for a population of 1,000,000, no patients with blast concussion were admitted to the hospital. Incidentally, the British had a rather good system of utilizing personnel, in that internists and neurologists tended to put borderline cases into the hands of physicians because the surgeons were too busy. One group of cases which was taken over by the neurologists was that of the closed head injuries. These cases went to neurologists or psychiatrists instead of to neurosurgeons. Neurologists and neurosurgeons were on the same floor in the hospital with which I was affiliated, and they worked in close association. There were no cases of blast concussion at all. The series included civilian cases and several hundred military cases from Europe and North Africa. Of course, in civilians there is not the urge to get away from the scene that there is in fighting personnel on the battlefield. Perhaps this is one reason that the civilians do not tend to behave in the way described by Commander Schwab. In general, civilians who were scared or ran about were treated unsympathetically, and they were no problem in the ward. The 1 patient during the war whom I saw acting thus was denounced by the other patients. There was no disciplinary problem for the staff.

To take up a more positive aspect of air blast concussion, and to cite a few extraordinary cases, I may first refer to the statement that such a concussion cannot occur in an open space, outdoors. The most striking episode I know of was reported by Surgeon Rear Admiral Cecil P. G. Wakeley. It concerned a yeoman of signals, who was standing on the bridge of a boat when a bomb hit the boat well forward in the bows and killed a number of men. No one on the bridge felt anything except this yeoman, who had pain in his foot. He reported it to his officer, who told him to continue his work. The yeoman did so but, glancing down at his shoe, noticed blood coming out over the top of it. When the shoe was removed, the anterior third of his foot came away with the shoe; it had been sheared off without visible damage to the shoe. He was standing on some grid work, so that the air blast may have sheared his foot off.

There is an amusing case in the literature in which one can rule out psychoneurosis. The subject was a pheasant. Stewart, Russell and Cone, of the Royal Canadian Army Medical Corps, several hours after bombs had struck outdoors, saw a pheasant standing several feet from a bomb crater, with its eye closed. They could walk over, pick up the pheasant, put it down and push it, and it would take a few steps. It tended to keep whatever position it was put into. It reacted in a waxy, hypertonic fashion. It was not observed again for a long time because the game warden took it. However, when it was killed, a number of hemorrhages were observed in the frontal region of the brain, but there was no damage to the scalp or the skull.

At the Canadian Neurological Hospital they had several cases of a condition which they considered true air blast concussion. The symptoms were apathy,

depression and indifference to surroundings. In some cases the spinal fluid was xanthochromic.

Effects of blast can be exceedingly bizarre in the absence of any damage. There is a well authenticated case, described by Denis Williams, of a man who was sitting on a several thousand pound bomb, doing something to it, when the bomb blew up. No one expected to find even a fragment of the man. However, after the smoke cleared away, the man was found wandering around rather dazed. He was sent back to England from Malta, but no evidence of injury from this episode could be found, and the man had no complaints.

DR. HENRY R. VIETS: I congratulate Dr. Schwab on this excellent paper, and I concur fully with his findings. One may compare, as he has done, the observations in this war with those in the last. In 1918 the diagnosis of "shell shock" was widely used and covered many types of reactions. Ninety-five per cent of them fell into the class of psychogenic mechanisms. The other 5 per cent were due to air blast concussions in a confined space, such as a dugout. In some of this small group of cases petechial hemorrhages were present in the brain. There were also cases of parkinsonism resulting from concussion. Only cases of this type of "shell shock" can be compared with Dr. Schwab's underwater cases. Certainly, in most of the cases in both wars the disturbances were psychogenic. In the first world war, however, there was much more gross hysteria than in the second.

Dr. Schwab stated that amnesia was relatively rare in World War I. There were many cases of prolonged amnesia, with fugues. Men wandered about France, lost for months or weeks, without any recollection of who they were or what unit they belonged to.

It is disturbing to think that, with all the work on this subject in the first world war, one should meet a situation in the second war in which a diagnosis of air blast concussion was often made and patients treated as surgical emergencies.

DR. HERBERT I. HARRIS, Portsmouth, R. I.: I saw a number of cases at Okinawa similar to those Dr. Schwab has described so well. I think it is well not to rule out the organic possibilities entirely in considering this syndrome. Conceivably, an air blast of sufficient speed striking the skull and body from one direction could produce sufficient motion of the skull to produce contrecoup. In the great majority of cases, however, the syndrome does appear to have its origin in the emotional sphere.

DR. PAUL I. YAKOVLEV, Waltham, Mass.: From Dr. Schwab's interesting paper it appears to me that the effects of blast are due chiefly to the violent sound effect. The sudden and intense acoustic stimuli have a peculiarly jarring and widespread effect on the entire organism, certainly much greater than the effect of a sudden flash of even blinding light. In this respect the anxiety-producing effects of sound have their nearest equal in the "shocking" effects of a suffocating, pungent smell. It is of interest that the central synaptic surface of the acoustic system, like that of the olfactory, and in contrast to that of the visual system, is peculiarly widespread. It consists of a great number of overlapping neurons between the receptor organ and the thalamus. The acoustic system is also one of the most important pace makers of the synaptic processes in the entire central nervous system. This is shown by the fact that some persons may be thrown into a violent epileptic fit by a sudden loud sound. The hyperacusis in congenitally decerebrate persons and in experimental animal preparations is also well known. It would seem reasonable, therefore, to assume that the intense sound of blasts, especially under conditions of great emotional tension, may cause lasting changes in the synaptic surface of the central nervous system and that the disturbances in the emotional-affective sphere, the vertigo, headaches and other symptoms, are due to these central effects, with or without an injury to the peripheral acustico-vestibular apparatus.

DR. G. COLKET CANER: I had the opportunity of seeing a number of these patients in a relocation center in Washington last winter. They were O. S. S.

men who had been dropped behind enemy lines and who worked with the resistance forces. Hardly any of them were subjected to severe shell fire. Practically all of them had the same syndrome. They were tense and restless, could not sit still long, were sleepless and had battle dreams and startle reactions. Many of them did not complain of symptoms in the field. They complained only after they had been out a week or more. While they were active and were using a great deal of energy, they were all right. When they got back to a quiet place, they became upset. This observation made me wonder whether the stress they had been under had overactivated the adrenal mechanism. The patients I saw quieted down after a number of weeks, but it took them quite a while to get straightened out. I wonder how much good it would have done them if they had been forced to recall their experiences under sodium amytal narcosis. If it was stress that made them sick, I should think that the stress of recalling their experience would have made them worse. It seems to me that it is the suggestions given while the patient is under sodium amytal narcosis that help, not the recall of traumatizing experiences. I should like to ask Dr. Schwab what he thinks about this.

DR. IVES HENDRICK: The subject is especially of historical interest, though it is a regrettable commentary on professional inertia that the history of shell shock revealed as a psychologic disturbance primarily motivated by anxiety should have to be repeated in the present war. Not until after the war is ended is there full recognition of the proper medical attitude toward these casualties.

Dr. Lawrence Kubie told me a most interesting detail of a careful investigation of these cases by abreaction methods; it was shown that the flash and light of the exploding shell was vividly recalled, but the sound of the explosion rarely, if ever. This observation may be unsubstantiated or may have been an artefact, but it suggests the possibility that this interval between perception of light and perception of sound represents the time during which amnesia sets in and, further, the possibility that any mental event so rapid as this may have its physiologic component.

Dr. Viets's comment on the differences in the syndrome in the two wars brings up an interesting aspect of psychologic and sociologic relations. It is undoubtedly true that although the basic phenomena of psychoanalysis are the same in different cultures, or in different periods of a culture, they give rise to different symptom formations. The most striking example of this is the rarity today of the major hysterias described by Charcot; so, in civilian practice one rarely sees major hysteria today, and the combat conditions of this war did not produce the combat neuroses of the last.

DR. JACOB E. FINESINGER: The fact that these patients with "concussion" show hyperactive reflexes and vasomotor instability, as do patients with combat fatigue, makes one wonder whether these patients have neurologic damage. I wonder whether one may not be dealing with a reaction which is in some instances irreversible. I am not sure whether available methods of examination are accurate enough to differentiate between no damage and slight damage to the brain. This differentiation is easier with patients who show evidence of distinct damage to the brain. In the last war some psychiatrists expressed the belief that a wound protected the patient from psychoneurosis. I should be interested in knowing whether a past history of psychoneurosis could be obtained from these patients with "blast concussion."

COMDR. ROBERT S. SCHWAB (MC), U. S. N. R.: The first point to be discussed is that brought out by Dr. Sweet concerning fractures of the ankle. He spoke of men who were standing on the deck of a ship and sustained such injuries when a bomb exploded nearby in the water. The Navy Department investigated a large number of these cases of fracture and found that the force of the explosion communicated to the ship through the water compressed the sides of the ship sufficiently to cause a sudden buckling effect on the deck, which was enough to fracture the foot of a man standing upright but would not fracture his bone if he were in a crouching position. This has nothing to do with air blast concussion, as the effect

in the case of fracture is transmitted through the water and the metal of the ship directly to the subject's foot. With respect to Dr. Sweet's comment on the pheasant and its neuropathologic changes, I can only state that I have read the article, and since it contained no accurate information about how the pheasant was injured I do not believe it proves anything. The bird might have fallen on its head. In answer to Dr. Viets, I stated that in these cases of so-called blast hysteria amnesia was present to a certain degree in 90 per cent, whereas the incidence was not so high as in the cases of shell shock reported in the literature. Dr. Harris' reference to the contrecoup effect is covered in Dr. Denny-Brown's review of the subject; it was felt that movements of the head with velocities great enough to produce this effect were not found in cases of air blast in either human subjects or experimental animals.

Dr. Yakovlev stressed the danger to the hearing apparatus. The journals of otolaryngology are full of reports of such damage, consisting of deafness, ruptured ear drum membranes and tinnitus. In most of the cases reported there were no neurologic or psychiatric symptoms. In the cases that I have described there were no such symptoms.

Dr. Caner's point is an interesting one. Pentothal has been helpful in cases in which there is not amnesia but repressed material of another sort.

Dr. Hendricks' comments were most interesting to me. In my interviews, a great many of the patients recalled the sound of the shell after the pentothal narcosis. However, they remembered much more vividly a flash of light, and the sound memory certainly was not the acute part of it.

I agree with what Dr. Finesinger says about a physiologic mechanism. I hope one will soon know whether or not abnormal emotional reactions are identical with abnormal physiologic states. A large number of these men, about 60 per cent, who suffered from this symptom had had neurotic episodes in their past lives. No doubt, if they had been interviewed in more detail as were those at the Massachusetts General Hospital by Dr. Finesinger a higher percentage of neurotic histories might have been obtained. It is important to emphasize that large numbers of troops went through the same amount of gunfire and did not break down, but continued to fight. I remember a soldier from the south who had the diagnosis of blast concussion on his card and who had amnesia. Under pentothal narcosis, he said that when the first shell went off and covered him with dirt he was in a place which was too dangerous for him to stay in. Another shell went off, and he lost consciousness. A third shell woke him up, and he crawled back to the aid station, where he fainted. It is difficult to see how the same physical trauma could produce amnesia on one occasion and an awakening on another unless it was through a psychologic mechanism. In many of these cases the patient had never been exposed to shell fire but the symptoms were produced from terrific emotional trauma alone.

In summary, I should like to emphasize again that it is possible to have damage to the brain from air blast, and, although there are undoubtedly cases of true concussion that have occurred, usually in confined spaces, over 90 per cent of cases are of the same pattern of the acute hysterical-anxiety symptoms one sees in other forms of sudden and acute emotional breakdown and the condition should be treated as a neurosis rather than as an injury to the brain. Some cases, to be sure, are of mixed type, with physical trauma, either head injury or damage elsewhere, associated with the neurosis. I have excluded these cases from my series whenever possible because of the complication of physical injury. I saw many cases of acute disorders on the beach in the Leyte campaign. They were identical with these cases of "blast concussion," but the condition was called battle fatigue. Whatever the diagnosis, the most efficient way of treating a patient with a war neurosis is to keep him in the combat area and treat him immediately. If he has a surgical condition, such as concussion, he must be evacuated to the rear; treatment, therefore, is postponed, and his chances of recovery are reduced.

Kenneth J. Tillotson, M.D., *Presiding*

Regular Meeting, Feb. 21, 1946

Mental and Performance Testing of Neurologic Patients. DR. EDWIN M. COLE, MISS MIRIAM P. BAGGETT and MISS MARJORIE R. MACMULLEN.

The work to be reported here is being carried on at the Massachusetts General Hospital, in an attempt to establish a testing program for use with neurologic patients and to obtain a battery of tests that will be useful in detecting impairment and will furnish a quantitative evaluation of impairment and a permanent record.

Many theories have been presented with respect to the type of loss or impairment characteristically present in organic disease of the brain. In general, loss seems to be greatest in memory and in functions or tasks which require spontaneous application of new concepts. Impairment being loss from a previous level of functioning, the task of measurement is made difficult by the need of a means of evaluating previous levels and capacities.

The present study is based on results obtained from 129 of 325 patients tested. Subjects were selected as a random sample from the neurologic wards of the Massachusetts General Hospital, and those included in this study were all between the ages of 15 and 59, inclusive; all were given both the complete Wechsler-Bellevue and the complete Hunt-Minnesota test, with a Wechsler-Bellevue score of 80 or above; and for all a relatively clearcut diagnosis on discharge was available from the clinical record. The cases were classified as follows:

I. Primary pathologic processes of the brain, i. e., changes involving the substance of the brain itself, such as toxic and degenerative conditions, infarctions, tumors and abscesses.

A.	Cerebral disease: 24 cases	
	Toxic delirium	2
	Head injuries (post-traumatic cerebral syndrome and contusion of the brain)	8
	Extrapyramidal disease (Wilson's disease, encephalitis and birth injury)	4
	Encephalopathy or increased intracranial pressure of unknown cause	2
	Cerebral degeneration (?), Alzheimer's disease	4
	Cerebral infarction	3
	Porencephalic cyst	1
		24
B.	Tumor and abscesses of the brain: 32 cases	
	Unlocalized or suspected cerebral tumor	15
	Specifically localized tumors and abscesses	17
		32
II.	Intracranial disease exclusive of cerebral tumor: 32 cases	
	Epilepsy	16
	Diseases primarily of the meninges	6
	Extracerebral, but intracranial, tumors, meningiomas and osteomas	10
		32
III.	Control group: 41 cases	
	Neurologic conditions without cerebral involvement	33
	Psychoneuroses	5
	Hypertension	3
		41

A careful history was obtained from all patients with respect to native tongue, educational level and language dominance. Tests used routinely included the Weschsler-Bellevue test for mental ability; the Hunt-Minnesota test for visual and auditory learning; Stanford achievement tests for reading, spelling and arithmetic; motor performance tests (including habitual skills, judging weights and test 5 of the Detroit tests of learning aptitude), and language tests.

Results.—Statistical analysis has shown that the groups tested were well matched as to age, the mean being 35 years; educational level (grade 9); intelligence quotient, and vocabulary level. Therefore, significant differences are apparently due

to a pathologic condition rather than to differences in age, education or intelligence quotient.

A significant difference between groups was found in the Hunt-Minnesota test as follows:

Group	Percentage with Pathologic Scores in Hunt Test
Cerebral disease	71
Cerebral tumor	61
Intracranial disease	57
Control	39

There was also for this test a statistically computed significant difference between mean scores for the group with cerebral disease and the control group, for the group with cerebral tumor and the control group and for the group with intracranial disease and the control group, although the ratio for the scores of the last two groups was significant only at the 0.05 level. The test neither eliminated all controls nor detected all cases with pathologic conditions, but the difference between group scores is sufficient to indicate that the test was effective significantly above the level of chance in discriminating between groups. Work with the Wechsler-Bellevue test showed that comprehension, digit symbol and picture completion tests were the tests most likely to indicate a pathologic condition.

Briefly stated, the results are as follows: For the group with cerebral disease, the scores for the comprehension and digit symbol tests differed significantly from the scores for the other subtests; for the group with cerebral tumor, the scores for the picture completion test, in addition to the scores for the comprehension and digit symbol tests, differed significantly; for the group with intracranial disease, the scores for the digit symbol and picture completion tests showed significant differences, but the score for the comprehension tests did not. The control group showed no consistent pattern of significant differences, and no subtest gave scores which differed significantly from the score for the comprehension, the digit symbol or the picture completion test. From such results it should be possible to establish differential scores that would provide quantitative indicators of the presence or absence of pathologic changes and the type of the pathologic process.

Of the standard achievement tests given, the spelling test proved most indicative. The control group demonstrated a normal curve for decline with age, while both the group with cerebral disease and the group with cerebral tumor measured reading comprehension and arithmetic computation at essentially equal levels, but spelling scores showed a conspicuous drop, especially in the group with cerebral disease. The group classified as having intracranial disease scored on spelling tests above the level of the other functions. This difference in pattern may, therefore, be considered in evaluating a total battery of tests.

In patients with organic disease of the brain, speed of performance was found to be diminished. In the use of tests requiring speed in performing habitual skills no significant differences were found between groups; that is, slow performance did not correlate significantly or consistently with pathologic change. In the Detroit Motor Speed Test in which precise pencil work is required, the patient used both the preferred and the nonpreferred hand, and the test was of interest in comparing the two sides rather than in determining speed, since, again, no group showed a consistent pattern. In judging weights, the most interesting finding was that ability to judge relative weights seemed to be correlated with the intelligence quotient.

A simple test, devised by Wells, for language disturbance was used in the form of comparing speed required for reading a list of words with speed required for naming colors. A ratio was obtained, and tentative norms were established. As with other tests which are without previous norms, further data must be accumulated, but the results suggest that the test is of use in detecting the presence of aphasia.

As a result of this work with a group of neurologic patients, the following conclusions can be drawn: 1. A clearcut quantitative record of the patient's abilities at the time of examination is obtained. 2. Variations in types of performance in terms of these tests are found with various pathologic processes, and these obser-

vations have been applied to the diagnosis for the specific patient. The results were particularly significant in cases of tumors of the brain substance and non-expanding lesions of the brain. Many extensive correlations need to be made, particularly with respect to other diagnostic procedures, such as examinations of the spinal fluid; ventriculographic, roentgenographic and electroencephalographic studies, and careful pathologic examinations, all of which, it is hoped, can be done in the future.

DISCUSSION

DR. F. L. WELLS: The amount of work represented in a special presentation such as this can best be appreciated by other workers in that specialty, and from this standpoint it has been a treat to listen to this paper, with its additional evidence that clinical psychometrics is getting beyond the "bug-hunting" stage of scientific observation, into the stage of systematic comparisons. To the sympathetic critic, the first suggestion of such a presentation is always, "Where does one go from here? What leads are opened up? How can one now do this better as a result of what has been done?"

As time goes on, the groups will of course be enlarged, which may somewhat modify the present indications: One thinks in this connection of the possibility of controls with other than neurologic diseases, after the manner of the work by Weisenburg, Roe and McBride in establishing adult norms for various intellectual functions. A research of this kind is not dependent on external norms and, having its own controls, is also independent of procedures developed elsewhere, and for other purposes. It seems quite likely that such procedures can be usefully refined on the basis of leads here given. There are some points at which item analysis may be useful—for example, in the Bellevue Information Test, the population of the United States, the discoverer of the North Pole or the definition of a thermometer; in the comprehension test, the reason that persons born deaf are unable to talk, or the likeness between a wagon and a bicycle. Moreover, unless evidence has appeared to the contrary, it might be well to inquire as to the differential performance with digits forward and backward, since the processes involved are very different.

It is perhaps not too early to consider some of the broader meanings of these observations. Until one has some notion of the reasons for these significant differences (and let it not be forgotten that statistical significance is not at all the same as pragmatic significance) one is on rather precarious interpretative ground, like the self medicator whose death was due to a misprint. How far is failure in the Bellevue comprehension test a reflection of poor judgment, or failure in the digit-symbol test a reflection of slowness in establishing new associations? Recently a close association has been posited between lowered digit span and anxiety, but other conditions may lower it quite as effectively. Anything will lower digit span that disturbs the capacity for controlled attention over short intervals; this is the essential thing to understand. One is justified in looking askance at test "profiles" of schizophrenia, organic conditions and the like. If schizophrenia, for example, really has any clearcut clinical meaning, and one understands that meaning, one will not need anyone to say whether or not some Bellevue response pattern is consistent with that meaning, and individual items of response will tell one far more about the presence of schizophrenic features than a pattern of subtest scores can possibly do. In attempting to understand what more general mental features these anomalies of test response have picked up, one will be in a situation to construct instruments of much greater effectiveness in spotting them.

A colleague of mine is, of course, in a different position, but I have often said that I would never let a student of mine get away with citing a global Bellevue intelligence quotient. Something was said about the correlation of weight perception with the intelligence quotient. One might consider whether it is not the higher mental processes which are involved in these discriminations generally, rather than any sensory factor. Indeed, the number of cases almost suggests another explanation, paralleled in an observation I recall with a small group of student

nurses, in which scores on the old Army Beta test had a correlation of about 70 with the alphabetical order of the names.

DR. EDWIN M. COLE: I wish to thank Dr. Wells for his discussion. He has given us much advice and many suggestions helpful in establishing our laboratory.

My intent has been to work out a test program which could be applied to a large number of neurologic patients. I felt it should be possible by means of these tests to pick up some cases of aphasia in the earlier stages, before they are otherwise readily observable. The tests must be applicable also to patients who have not had great experience or training in the use of English. Finally, since such a battery of tests is to be widely used and since the time allowance per patient is short, one is necessarily limited as to the amount of detail in such an examination.

Neurologic patients without apparent cerebral involvement were used as controls, since it seemed wise to use the same type of patients exposed to the same sort of conditions as control material.

Occlusion of the Basilar Artery: A Clinical and Pathologic Study. DR. CHARLES S. KUBIK and DR. RAYMOND D. ADAMS.

This paper will be published in full in *Brain*.

MICHIGAN SOCIETY OF NEUROLOGY AND PSYCHIATRY

Thomas J. Heldt, M.D., *President, in the Chair*

Regular Meeting, Detroit, Oct. 17, 1946

Protrusion of Cervical Intervertebral Disk. DR. ALBERT S. CRAWFORD and DR. HAWLEY S. SANFORD, Detroit.

Our present interest in the syndrome of cervical intervertebral disk stems from the report of Semmes and Murphey, who, in 1943, pointed out that disk material in the cervical area will often protrude laterally and not necessarily encroach on the spinal cord (Semmes, R. E., and Murphey, F.: *J. A. M. A.* **121**:1209, 1943). A monoradicular syndrome results. The present report adds 9 cases with operation to the literature. These 9 cases represent less than one third of the cases in which this diagnosis was made at the Henry Ford Hospital during the previous nine months.

There are several similarities between protruded disk in the cervical region and that in the lumbar area. In the cervical area the lower interspaces are usually involved, as they are in the lumbar region. These two areas are the points of maximum motion in the spinal column. Trauma plays an etiologic role in protrusion of cervical disk, although it may not be so violent or so well remembered as the trauma which precipitates a protrusion of the lumbar disk.

After the original injury, there follow "cricks" in the neck, which are reminiscent of the attacks of lumbago preceding the first attack of sciatica. In the cervical area, straining, coughing and sneezing will also aggravate the pain. Division of the scalenus anticus muscle, which may be in spasm, often gives temporary relief from the pain following protrusion of a cervical disk, similar to the results following Ober's operation for herniation of a lumbar disk. Doubtless, in the past, protrusion of a cervical disk has been diagnosed as the scalenus anticus syndrome, as well as brachial neuralgia due to arthritis of the cervical portion of the spine.

The characteristic monoradicular syndrome for herniations of the fifth and sixth cervical disks was described. The technic of the "foraminal compression test," as described by Spurling, was emphasized, with special attention to keeping the neck hyperextended as well as tilted. This test should be made with caution, and preferably only once on any one patient.

Contrary to some reports, myelography is quite satisfactory in demonstrating protrusion of cervical disk. It is of importance to use enough "pantopaque" (a

mixture of ethyl esters of isomeric iodophenylundecylic acid), preferably 6 cc., the needle being introduced in the fifth lumbar interspace. After the "pantopaque" has been injected, the head of the fluoroscopy table is lowered, the patient's neck hyperextended and the medium allowed to pool in the cervical part of the spinal canal. The defect is usually demonstrated satisfactorily. It has been found that the "pantopaque" is removed most rapidly with the cooperation of the patient and the examiner. The patient repeatedly performs the Valsalva maneuver, trying forcibly to expel air against his closed air passages. This supposedly causes engorgement of veins in the epidural space. At least it compresses the dural sac and causes the "pantopaque" to flow out through the needle. At the same time, gentle suction is made by syringe. With this method we have been able to remove practically all the "pantopaque" which can be seen fluoroscopically.

The symptoms of protrusion of cervical disk seem to be relieved more readily by nonoperative measures than is true of the symptoms following protrusion of lumbar disk. Perhaps this is due to the structures, namely, tendons and muscles, being smaller in the cervical area and more influenced by stretching procedures. Our present mode of therapy is daily diathermic applications to the cervical muscles, followed by four or five "pull-ups" of five minutes each in the Sayre halter traction. This treatment should be continued for at least two weeks. Traction of the neck at night seems to have little value.

In reviewing the surgical considerations, several anatomic factors are considered, particularly the narrowing of the foramens in the dorsoventral plane, the relative crowding of the cervical portion of the canal with nerve tissue and the close approximation of the nerve roots to the disk in the lower cervical region. Two types of pathologic changes are encountered: (1) hard (segment of annulus detached), with a clearcut history and findings, and (2) soft (nucleus pulposus), with a history of intermittent symptoms and insidious onset with respect to location; the central type is usually larger and more likely to give signs referable to the cord, while the lateral type is smaller and is likely to give few or no such signs but is characterized rather by local signs and disturbances referable to the nerve root.

The indications for surgical exploration are (1) recurring attacks with increasing severity of pain; (2) failure to respond to conservative management in two or three weeks; (3) progression of sensory and/or motor signs; (4) chronic state, with signs of localized pressure on a nerve root. Exposure is made by hemilaminectomy with the use of local or general anesthesia, and sufficient bone is removed to facilitate excision of the protruded segment and to give adequate decompression of the involved nerve root.

The results are satisfactory in the majority of cases. First, pain disappears; then the sensory and motor functions return to normal. The time required depends on the extent of the lesion and the duration of involvement at the time of operation.

Protamide Therapy for the Pain of Tabes Dorsalis. Dr. Russell T. Costello, Detroit.

This article will be published in another journal.

NEW YORK NEUROLOGICAL SOCIETY

Joseph H. Globus, M.D., *President, in the Chair*

Regular Meeting, May 7, 1946

Dumb-Bell Tumors of the Spinal Cord: Report of Two Cases. Dr. Bernard C. Meyer (by invitation).

Two patients showing extramedullary tumors of the cervical portion of the cord with atypical features were presented from the neurologic service of the Mount

Sinai Hospital (New York). The first, a 20 year old student, first noticed numbness and dysesthesia of the right hand one year before hospitalization. Later stabbing pains began in the right arm. Later, numbness of the right side of the trunk developed, followed by a swollen feeling in the right foot. These symptoms were accompanied with difficulty in using the right arm and in walking. Examination revealed mild right hemiparesis, involving more especially the upper limb; signs on the right side referable to the pyramidal tract and impairment of deep sensibility on the same side. A level of hypalgesia and hypesthesia was noted at the fourth cervical and, again, at the third dorsal dermatome, especially on the left side, indicative of partial Brown-Séquard syndrome. Studies of the spinal fluid revealed no block; the protein content was 12.6 mg. per hundred cubic centimeters. Roentgenographic examination of the cervical portion of the spine disclosed destruction of the right lamina of the fifth vertebra with some involvement of the body of the vertebra. Laminectomy revealed a dumb-bell-shaped tumor arising from the fourth anterior root; the growth was both intradural and extradural. The extradural part, extending through the intervertebral foramen, was about twice the size of the intradural portion. Recovery followed the removal. The tumor proved to be a neurofibroma.

The second patient, a housewife aged 36, was admitted to the hospital one year after the onset of fatigue and paresthesias in the fingers of the right hand, which was followed by transient weakness of the legs. Weakness of the arm continued and was followed by numbness of the right side of the chest and later by weakness of the right leg. Examination revealed weakness of the right arm with some winging of the scapula. Signs referable to the pyramidal tract were noted in all four limbs, chiefly on the right side. Vibratory sense was absent in both legs and diminished in the right arm. Analgesia was present on the right side from the fourth cervical to the tenth thoracic dermatome, below which a zone of hypalgesia extended to the third lumbar dermatome. The right pupil was narrower than the left. There was no spinal fluid block, and the protein content was normal—46 mg. per hundred cubic centimeters. Postoperative roentgenologic studies of the cervical portion of the spine, originally considered normal, revealed destruction of the laminas of the second vertebra. The symptoms fluctuated during the early part of her hospitalization. Myelographic study was unsuccessful. Despite the uncertainty of the diagnosis, exploration was attempted. On two occasions, however, the patient went into shock, even before anesthesia had been started. On a third attempt, despite a systolic pressure of 60 mm., the operation was begun, exposing a large extradural tumor in the upper cervical region, which at the level of the second cervical vertebra was even extravertebral. The tumor extended intraspinally anterior to the dura. Severe hemorrhage necessitated closure, which was followed by quadriplegia. One week later the entire tumor was removed, which was followed by an excellent recovery. The tumor was a neurofibroma.

These cases are presented because, despite the generally accepted belief that extramedullary tumors of the cord are associated either with an increase in the protein content of the spinal fluid or with manometric block or with both, no abnormality of the spinal fluid was revealed in either. It is evident, therefore, that the absence of spinal fluid block or of elevation of the protein content does not exclude the possibility of extramedullary tumor of the cervical portion of the spinal cord.

DISCUSSION

DR. IRA COHEN: As Dr. Meyer pointed out, one not infrequently is put to it in the diagnosis of extramedullary tumors of the cord, particularly those of the high cervical region, which do not follow what one is pleased to call a typical pattern. The second case is a good example of this. The patient was under observation for three months; not only because of her peculiar behavior in the operating room prior to administration of the anesthetic, but also because of her possible improvement, we were loath to do an exploration; yet she had an extramedullary tumor, which was removed. The first case that Dr. Meyer presented

is of particular interest to the neurosurgeon, because a few days after operation spinal fluid accumulated in the tissues of the neck and there developed fever of unexplained origin, which occasionally occurs after suboccipital craniotomy. For several weeks the patient had a spiking fever, in spite of administration of various drugs (there was no infection, but he was treated as though there might have been). The collection of fluid disappeared suddenly, and the temperature dropped to normal and remained there.

As to dumb-bell tumors in general, there is nothing peculiar about them from the neurologic or the diagnostic standpoint except that they almost invariably give roentgenologic evidence of their presence. They may be extradural and intradural, or extradural and extravertebral or intradural and extravertebral. As a class they are not of particular interest from the diagnostic standpoint; neither are they of particular interest to the neurologist, but they are of interest to the neurosurgeon because of technical difficulties on the operating table, and they may well be of interest to the general surgeon.

I should like to show a roentgenogram of a patient who came with tremendous destruction of the cervical vertebrae, with a mass in her neck which was as large as a good-sized lemon. A biopsy had been done, but no attention had been paid to the rest of the neurologic signs. It is clear that dumb-bell tumors in the cervical region may well come under the care of a general surgeon, who should keep in mind that there is such a thing as an intraspinal extension.

This type of tumor may also be of interest to the thoracic surgeon. A patient may present such a tumor as this one, but with symptoms from the intraspinal part, and not from the part of the tumor in the posterior mediastinum. Such a tumor is the joint concern of the neurosurgeon and the thoracic surgeon. On the other hand, if there are no symptoms referable to the spinal cord, it can be tragic when the thoracic surgeon does not consider the possibility of a dumb-bell tumor, as was my experience when I was called to see a patient in another institution from whom a posterior mediastinal tumor had been removed. There had been some bleeding, and the surgeon had packed down to the bleeding point. When the patient awakened from the anesthesia, he was paraplegic. He had a spinal block, and I operated, thinking there had been displacement of the intraspinal part of the tumor; instead I pulled out the packing from the spinal canal which had been used to stop the hemorrhage. The thoracic surgeon must remember that a mass in the mediastinum may be connected with an intraspinal tumor. It may be that these dumb-bell tumors are not so infrequent as one is prone to think; among 110 extramedullary tumors, I have encountered 8 well defined dumb-bell tumors; so the proportion is a bit greater than is generally thought.

DR. LEO M. DAVIDOFF: These tumors can be extraordinarily benign. I encountered a case fourteen years ago, that of a middle-aged pharmacist, not unlike the second case reported here. There was severe hemorrhage at operation. These tumors grow out laterally and acquire a rich blood supply from the vertebral artery, and that is what happened in this case. I removed the intraspinal portion easily, but when I attempted to excise the extraspinal portion I was forced to stop. The patient improved after removal of the intraspinal part, and he is still maintaining his improvement, fourteen years later. He has never had the extradural portion removed, has had no other therapy and has returned to his job and continued working ever since. Thus, if the extraspinal portion is too vascular, it may not be a tragedy to let the patient retain his tumor and save his life.

Ophthalmoplegia with Reversal of Bell's Phenomenon Occurring in a Diabetic Patient. DR. EDWIN A. WEINSTEIN.

Bell's phenomenon is the associated upward rolling of the eyeballs that occurs with vigorous closure of the eyelids. It is particularly evident on the side of a peripheral paralysis of the facial nerve. Forceful closure of the eyelids is also associated with constriction of the pupil, which may be observed by holding the lids apart.

S. G., a housewife aged 32, was admitted to the Mount Sinai Hospital on Feb. 28, 1946, because of vertigo, diplopia and drooping of the left upper eyelid. The patient had been known to be diabetic since the age of 10 and had been admitted to the hospital on nine occasions, once in coma and several times for acidosis. She had been treated twice for bleeding from the gastrointestinal tract. Epistaxis was a frequent complaint, and it was noticed that the patient bruised easily. In 1943 she had an illness similar to the present one, when, after an infection of the upper respiratory tract, she complained of vertigo and diplopia. Examination revealed paralysis of the left external rectus muscle. The patient recovered completely from this episode, and her neurologic condition was normal until three weeks before the present admission, when she again experienced vertigo and diplopia after an infection of the upper respiratory tract. Examination on her admission showed the following abnormalities:

1. Pronounced arteriosclerotic changes in the retinal vessels with areas of degeneration and hemorrhage.

2. Complete ptosis of the left upper eyelid.

3. Paralysis of internal rotation and of upward and downward movements of the left eye.

4. Miosis of the left pupil, with a diameter of 1.5 mm., whereas the right pupil measured 4 mm. Both pupils failed to react in accommodation, whereas their reaction to light was brisk. Convergence was intact in the right eye.

5. No movement of the paralyzed (left) eyeball during elicitation of Bell's phenomenon, while the right eyeball moved down instead of up. The pupils did not contract, and at times the right pupil was seen to dilate.

The spinal fluid was clear, with a total protein content of 58 mg. per hundred cubic centimeters. Application of the tourniquet with a pressure of 100 mm. to the upper portion of the arm produced numerous petechiae within three minutes.

In the first few days after the patient's admission the left pupil gradually grew larger, so that it was 1 mm. larger than the right pupil. Two weeks after her admission the left levator palpebrae muscle began to regain power, and one week later the reversed Bell's phenomenon in the right eye had disappeared. When the right eye was closed forcibly, the right globe rotated upward and the pupil contracted. A pseudo-Graefe phenomenon was seen in the left eye, with improvement in the power of the left internal rectus muscle. When the patient looked to the right, the paretic lid rose. This persisted after all other ocular movements had been restored.

This case is presented for two reasons. First, it affords an excellent example of the lesions in the brain stem which are being encountered in young diabetic persons with increasing frequency. Second, it is of interest in connection with the clinical physiology of ocular movements. Patients with severe diabetes show a premature vascular aging. Many young diabetic patients who would otherwise have died have been kept alive with better means of administering insulin and more efficient measures of combating infection. Vascular damage is observed early in these patients. At the age of 19 and 20 changes in the retinal arteries and hemorrhages may be observed in the fundus. Diabetes affects mainly the finer vessels, so that involvement of the smaller vessels of the brain stem is comparatively commoner in diabetic patients than is thrombosis of the larger arteries of the cerebrum. In the experience of my associates and myself, diabetes has replaced syphilis as the most common agent in vascular disease of the brain stem in young people. All are familiar with the frequency with which diabetes is the cause of thrombosis of the posterior inferior cerebellar artery. The pons and midbrain may also be affected, as this case illustrates.

Bell's phenomenon, as well as other acts involving integration of the various cranial nerves, may be reproduced experimentally by electrical stimulation in the region of the central tegmental fasciculus (Weinstein, E. A., and Bender, M. B.: Integrated Facial Patterns Elicited by Stimulation of the Brain Stem, ARCH. NEUROL. & PSYCHIAT. **50**:34 [July] 1943). Stimulation of the oculomotor or the

facial nerve or nucleus did not produce the phenomenon, nor could it be elicited from those cortical areas which produce closure of the eyelids. Its reversal thus furnishes presumptive clinical evidence of an intramedullary lesion of the brain stem.

DISCUSSION

DR. MORRIS B. BENDER: This paper brings to my mind several phenomena. As Dr. Weinstein stated, the so-called Bell phenomenon is a part of the associated movements of the eye occurring in closure of the eyelids. With closure of the eyes there is upward movement of the globe (Bell's phenomenon) and contraction of the pupil. In studying these movements in the monkey under experimental conditions, Dr. Weinstein and I were able to reproduce them by stimulating the central tegmental fasciculus. We tried to abolish Bell's phenomenon by destroying this area in the brain stem, but we were not successful. All we found was that the eyeball did not move completely upward; there was a slight movement above the horizontal meridian.

Dr. Weinstein also mentioned the pseudo-Graefe phenomenon. This is synkinetic retraction of the superior lid whenever the subject attempts to look down. As a rule this is due to a lesion in the oculomotor nerve. However, Dr. Weinstein said he believed that in this case the lesion was intramedullary, and I agree with him. The pseudo-Graefe phenomenon may occur with intramedullary lesions. I think its occurrence may be explained by taking into consideration what Dr. Walter Cannon called the law of denervation. This law was first postulated by Claude Bernard. He stated that once an organ is denervated it becomes extremely sensitive. It reacts to various stimuli whether natural (neural), chemical or mechanical. This law of denervation applies to peripheral organs as well as to the structures within the central nervous system.

It is known that if one cuts the oculomotor nerve, after a varying period, the oculomotor muscles become very sensitive to the action of acetylcholine and that when there is recovery of function it is very hard to get contraction of an individual muscle. The same is true for lesions of the facial nerve supplying the facial musculature. After lesions of these nerves most of the recovered movements are synkinetic. The synkinesias in the case of the oculomotor muscles may be due not only to indiscriminate regeneration of the oculomotor nerve rootlets within the midbrain, but also to increased sensitivity of the ganglion cells in the oculomotor nucleus. The increased sensitivity of the ganglion cells in the oculomotor nucleus may be due to a partial denervation as a result of the intramedullary lesion.

Analogous to the denervation of the cells of the oculomotor nucleus is that of the ganglion cells within the anterior horn as a result of lesions in the corticospinal tract. This, according to Cannon, may explain the increase in the tendon reflexes associated with lesions of the corticospinal tracts. The law of denervation, as postulated by Claude Bernard, should be seriously considered and investigated further, as suggested by Cannon. I am sure many puzzles in neurology would be cleared by such a study.

Origin of Tumor of the Midbrain. DR. J. M. FRIEDMAN (by invitation) and DR. L. GREENSTEIN (by invitation).

This paper will be published in a future issue of the ARCHIVES.

DISCUSSION

DR. JOSEPH H. GLOBUS, New York: Most neurologists are familiar with the fact that true tumors of the midbrain are rare, and I have often wondered why this is so. But before one can explain the infrequency with which they occur, it is necessary to establish the source of the formation of tumors in this region. A search of the embryonic factors gives satisfactory information. Developmental defects in the region of the aqueduct of Sylvius and blastomatous changes result in tumors, which, in turn, cause atresia of the aqueduct of Sylvius. Familiar also is another, more frequent, malformation in the aqueductal region, the so-called

stenosis, or atresia, of the iter, for which, though its existence was known for many years, almost a century, no satisfactory explanation has been advanced. It was thought this atresia was due to an acquired inflammatory disease, but I think that now the explanation has been found. The developmental defect which causes blastomatous changes, resulting in tumor formation, is also responsible for the aqueductal atresia seen in the newborn.

Why should tumors of this type be rare? In all probability the atresia occurs so early in the development of the organism that a fatal termination interrupts the process of tumor formation. On the other hand, the subependymal matrix in this region is relatively poor in cellular material, and the embryonic changes in the course of development are few; therefore the occurrence of blastomatous formations in that region is rare.

DR. LEO M. DAVIDOFF, New York: I can only confirm the statement that the occurrence of primary tumors in this region is rare.

Encephalopathy (Kernicterus) of Erythroblastosis Fetalis: Serologic Diagnosis and Pathogenesis. DR. ALEXANDER S. WIENER (by invitation) and DR. MATTHEW BRODY (by invitation).

During the past forty years there have been many clinical and pathologic studies of kernicterus, most of them describing a severe or fatal neurologic syndrome as a complication of a neonatal jaundice in infants with normal parents. Until recently there was no adequate explanation of this peculiar combination of cerebral and hepatic disease. By ascribing the disorder exclusively to the cholemia one could not account for the fact that with the severe jaundice of congenital atresia of the bile ducts kernicterus does not occur. With the discovery of the Rh factor (Landsteiner, K., and Wiener, A. S.: *Proc. Soc. Exper. Biol. & Med.* **43**:223 [Jan.] 1940), which was shown to be responsible for almost all intragroup transfusion reactions (Wiener, A. S., and Peters, H. R.: *Ann. Int. Med.* **13**:2306, 1940), Levine and associates suggested that the Rh factor was the antigen at fault in erythroblastosis (*J. A. M. A.* **116**:825 [March 1] 1941).

If an Rh-negative woman marries an Rh-positive man and has an Rh-positive child, in the great majority of cases no sensitization occurs. In 1 or 2 cases out of 50, the mother becomes sensitized, either through childbirth or through a previous transfusion with Rh-positive blood. Each subsequent pregnancy may increase her sensitivity. The antibodies produced traverse the placenta and produce one or another manifestation of erythroblastosis in the infant, or a stillbirth. While the Rh factor is responsible for the disease in 90 per cent of cases, in 10 per cent the ordinary A and B blood group factors or the Hr factor produces the sensitivity. It becomes evident that the mere demonstration that the mother is Rh negative and the infant, whose neurologic disorder or mental deficiency is ascribed to the Rh factor, is Rh positive proves nothing, since sensitivity only infrequently follows in such instances, and since sensitivity can also occur as a result of factors other than Rh. In order to prove serologically that such sensitivity exists, it is necessary to demonstrate in the blood of the mother antibodies that react with factors in the infant's blood. Recent work indicates that there are two main types of antibodies. One is bivalent in the chemical sense and causes agglutination. The other is univalent and requires special technics for its demonstration. We have found that in practically all our cases in which kernicterus or neurologic sequelae occurred we could demonstrate the presence of bivalent antibodies (agglutinins) in the blood of the mother. This led to the hypothesis that the type of the antibody determined the nature of the disease. Our theory proposes that agglutinins formed in the mother's serum traverse the placenta chiefly during the muscular activity of birth and produce agglutination thrombi in the vessels of the infant where circulation is slowest. In the lung, such agglutination thrombi can produce pulmonary hemorrhage. In the bone marrow, these agglutination thrombi stimulate the formation of erythroblasts, even in the absence of anemia. In the liver, they result in increased jaundice. In the brain, the agglutination thrombi cause damage to and

destruction of tissue. The damaged and destroyed brain tissue then picks up the bile pigment. Thus, jaundice of the nuclear masses of the brain (kernicterus) is the result of an in vivo staining reaction and is in itself of little clinical importance. We feel that it is the widespread damage produced by the agglutination thrombi in the brain that is important. Postmortem examinations in 3 cases of kernicterus seem to confirm our theory.

For the sake of completeness, it may be said that the univalent antibodies—glutinins, or blocking serums—are smaller and traverse the placenta earlier in pregnancy, producing hemolytic anemia and hydrops fetalis without neurologic sequelae. If dehydration is present, then univalent antibodies may produce conglutination in vivo, with results akin to agglutination.

Examination in 3 cases of hepatolenticular degeneration failed to demonstrate any evidence of isoimmunization. Our theory, then, does not account for all instances of hepatic-cerebral disease.

This paper was published in full in the July 1946 issue of the *American Journal of Mental Deficiency*, pages 1 to 14.

DISCUSSION

DR. TRACY J. PUTNAM: I have learned a great deal from this admirable paper, the conclusions of which seem to me to be conservative. I am not competent to discuss the serologic aspects of the paper, but there is in my mind no doubt that the slides show obstruction of the venules and capillaries which is sufficient to account for the lesions, and it seems to me there is much to be said for the thesis that this obstruction of vessels leads to the necrosis, or partial necrosis, of the basal ganglia, and that this is a sufficient explanation of the yellow staining of the basal ganglia in these cases. I once had the opportunity of studying a case of carbon monoxide poisoning which offers interesting parallels, for in this case the patient was treated with injections of methylene blue, or was given methylene blue intravenously, a form of treatment which was popular at the time. It was not life saving in this instance. However, the patient survived long enough for the methylene blue to produce an exquisite intravital staining of the necrotic areas in the basal ganglia and elsewhere, but not of the living brain substance. It was quite clear that the necroses were not confined to the basal ganglia. The basal ganglia were clearly necrotic; the tissue was definitely softened, and the structure could barely be made out. However, it was quite clear that the structure had many resemblances to the venules and capillaries that we have just seen. That is, the venules were enormously dilated beyond their ordinary proportions, and the capillaries were widely distended as compared with the normal size. In that case, and I believe in practically all cases of late death in carbon monoxide poisoning, there were also focal necroses in the white matter. These have not been widely emphasized, but they are practically always present; there is an example in MacCallum's "Textbook of Pathology" showing this phenomenon of striking necrosis in the basal ganglia with striking small necroses distant from the basal ganglia in the white matter, obviously of the same nature, for in the center of these areas of necrosis there is a distended, obstructed vein much as in those seen on the screen. In this connection, I should like to ask the authors whether they found any small areas of necrosis or of yellow staining in the white matter. I should expect it to occur in the white matter with this widespread necrosis of the basal ganglia. I may say that the specimens of kernicterus I have seen, which have not been numerous, have not shown as definite and striking a necrosis as is apt to occur with carbon monoxide poisoning. Certainly, the late effect, such as is seen in the encephalogram, would suggest that serious tissue damage had occurred, and it is possible of course that in the brains of babies dying shortly after birth there are widespread areas of cellular destruction without disintegration, and that the cellular disintegration is a late stage of this process. I should appreciate a further discussion of this point. I should also like to ask the authors whether, in their opinion, the same mechanism is responsible for the atrophy of the basal ganglia in other clinical types of disease of the basal ganglia, such as bilateral

athetosis and dystonia. The pathologic process is in some instances extremely obscure and vaguely suggestive of some such process as this. It is certainly not well explained by any theories yet proposed.

I am sure that the authors are right in attributing this peculiar localization to the unusual blood supply of the basal ganglia, which is striking in specimens injected with india ink or in those stained with the benzidine method. It becomes clear that the capillary architecture in the basal ganglia differs from that in any of the vascular areas of the cortex. In the cortex there is a gradual and early transition from one size of the small arteries to the arteriole, and so to the capillaries, and through the capillaries to the venules, and then to small and then to large veins. In the basal ganglia, however, it is striking that the capillaries are of extremely small caliber, just barely sufficient to transmit a red cell, that they spring suddenly from rather large arteries and end in moderate-sized veins; that is, arterioles and venules are comparatively sparse in the basal ganglia as compared with the cortical areas, and they are both quite different in structure from the extremely sparse vessels of the white matter.

Dr. Philip Levine (by invitation): Kernicterus is known only as a pathologic entity, but it now becomes important for the neurologist to see the erythroblastotic infants soon after birth for the detection of symptoms referable to pathologic changes in the brain. I share the view of the well known British pediatrician Dr. L. G. Parsons, cited in an editorial, published in the *British Medical Journal* (**2**:188, 1945) that if the diagnosis can be correctly made shortly after birth such an infant should not be treated but, rather, should be allowed to die.

The observations of Dr. Wiener and Dr. Brody have a certain amount of logic, but closer scrutiny of their views on kernicterus (Wiener, A. S., and Brody, M.: *Science* **103**:570, 1946) and of Dr. Wiener's entire concept of blocking antibodies and agglutinins reveals glaring defects. In the first place, the sections from only 1 case are presented, and if the agglutinative thrombi in the blood vessels of the brain represent the end result of a specific antigen-antibody reaction, such lesions should be demonstrated in many other tissues, particularly in the kidney. To my knowledge, oliguria, anuria or renal lesion, other than evidence of extramedullary hemopoiesis, has not been described.

Presumably, the authors are willing to gamble on observations in only 1 case. Were their views correct, kernicterus would be associated exclusively with erythroblastosis. However, this condition has been described by Dr. S. Farber, of the Children's Hospital in Boston, in patients who never had symptoms of this disease. In an oral communication, he tells me that a complete pathologic study of 55 cases of kernicterus failed to reveal the presence of agglutinative thrombi in the brain. Furthermore, Dr. Farber has observed kernicterus in premature and full term infants, irrespective of the presence of jaundice or erythroblastosis.

If agglutinative thrombi do represent the specific lesion in kernicterus, then one should expect a closer relationship of kernicterus to the presence of anti-Rh agglutinins in the mother's serum. In the first place, kernicterus is rare, while anti-Rh agglutinins can be demonstrated in somewhat better than 50 per cent of all Rh-negative mothers soon after delivery. A review of my own cases shows that the recovered erythroblastotic infants in the vast majority of cases in which the mother had powerful anti-Rh agglutinins remained normal and free from all symptoms. Furthermore, when the erythroblastotic infants did manifest symptoms of kernicterus, this development was not always correlated with the agglutinin titer. Finally, kernicterus was observed in instances in which the mother had no anti-Rh agglutinins but only blocking antibodies.

Aside from these considerations, Dr. Wiener's concept that anti-Rh agglutinins are of larger molecular size than blocking antibodies must be considered as purely hypothetic. One might expect to have heard from Dr. Wiener and Dr. Brody data on physical measurements of these contrasting antibodies, but, to my knowledge, all the evidence presented is indirect. Furthermore, passage through the placenta may depend on shape and electric charge of the molecule rather than on size.

The clearcut separation of forms of erythroblastosis on the basis of the presence of blocking antibodies or agglutinins cannot be confirmed by other workers in the field. I have seen infants with pure hemolytic symptoms in which the mother's serum showed the presence of strong anti-Rh agglutinins and no blocking antibodies. Dr. Wiener expresses the belief that in these cases only minute amounts of blocking antibodies could be held responsible for the hemolytic symptom, but the burden of proof of demonstrating the presence of weak blocking antibodies in a serum which shows a high titer of agglutinins and no zone phenomenon rests entirely on his shoulders.

Still more amazing is Dr. Wiener's use of the term "conglutination reaction" for the test with serum-suspended cells. In the first place, Dr. Wiener's concept of the elements in serum required to bring about the direct agglutination with blocking antibodies is vague and is entirely disproved by the fact that albumin-suspended cells are also active (Diamond, L. K., and Denton, R. L.: *J. Lab. & Clin. Med.* **30**:821, 1945). In the light of these facts, the term "conglutination" should be limited strictly to the phenomenon described by Bordet and Gay (Bordet, J., and Gay, F. P.: *Ann. Inst. Pasteur* **20**:467, 1906), a phenomenon in beef blood dependent on a heat-labile component. The use of the term "conglutination" for the direct reaction of serum, which was criticized also by British workers (Coombs, R. R. A.; Mourant, A. E., and Race, R. R.: *Brit. J. Exper. Path.* **26**:255, 1945) should be abolished. Actually, albumin-suspended cells are far more sensitive, and are therefore preferable (Levine, P.: Unpublished data).

Dr. Joseph H. Globus: In order to establish that a lesion exists in the brain when a vessel is occluded, it is necesary to demonstrate the existence of reactive phenomenon around that vessel. The brain is sensitive to occlusion of blood vessels, and when a vessel is occluded there is an immediate reaction around the vessel, expressed in accumulation of such elements as glial cells and macrophages. In the material presented here, I saw no evidence of reactive phenomena, and in their absence I cannot accept the fact that this occlusion of blood vessels has been actually demonstrated and that it played a part in the development of lesions which have not been demonstrated.

My associates and I have in our collection 6 cases of erythroblastosis. We have grouped them with the cases of kernicterus, but we noted that the icteric discoloration was not limited to the basal ganglia, but that the gray matter wherever it was found was affected in varying degrees. It is true that the gray matter on the surface of the brain was not affected as much as the basal ganglia, the inferior olives, the red nucleus or the gray matter of the cerebellum; but it is certain that this discoloration, this accumulation of pigment, was not limited to the basal ganglia. It was widespread, and cases were reported in which the gray matter of the spinal cord was equally affected. Moreover, in none of the 6 cases were neurologic manifestations exhibited in the nature of meningeal irritation or involvement of the cortex or basal ganglia. No cerebral lesions of any kind were noted in these 6 cases.

Dr. Leon H. Cornwall: I wish to endorse what Dr. Globus has said regarding the absence of areas of degeneration around the thrombosed blood vessels. I saw no such areas in any of the photomicrographs.

I wish to ask one or two questions. First, is the term "kernicterus" a desirable one to retain in the nomenclature? Many have long felt that neurology should function as the supreme commissar of the hierarchy that presides over medical diagnosis and therapy. In order to exercise our acumen in diagnosing correctly the disease under discussion, we, as clinical neurologists, must possess a degree of serologic insight sufficient to enable us to evaluate such tests as conglutination, blocking and agglutination, in order to determine the presence or absence of the Rh factor in mothers of prospective infants. Dr. Brody has urged us to become more interested in this disease in order that we may contribute of our diagnostic and therapeutic skill in caring for these unfortunate infants. I am somewhat confused, as is Dr. Globus, as to just how we are to make our diagnoses. It is my

understanding, and I believe that Dr. Globus is in accord, that the diagnosis has up to now been made only after necropsy. Such a situation, of course, puts the diagnostic ability of clinical neurologists to a severe test.

If I understood Dr. Brody correctly, he advised the removal of the offending isoimmune bodies by drainage. I do not know just how to do a venipuncture on an unborn infant.

For my second question, I want to inquire how he would suggest that we treat the erythroblastic infant prenatally after we have arrived at a diagnosis from serologic studies of the mother? Even more pertinent is the question how we are to arrange to have the mother come under our supervision in order that we may be enabled to treat her unborn offspring. All this should impress us with the rapid pace at which medicine is progressing.

DR. ALEXANDER S. WIENER: As I am not a neuropathologist, I must admit that some of the questions are too difficult for me to answer; I shall therefore confine my remarks to the serologic and clinical aspects. We have good evidence now that the placenta can act as a filter for separation of various sorts of antibodies, because it lets blocking (univalent) antibodies through, but not agglutinating (bivalent) antibodies. This explains the clinical observation that the severity of the disease in the infant (or fetus) is correlated with the maternal antibody titer in the case of univalent antibody disease, but not in the case of bivalent antibody disease.

While it is believed that the agglutinins are milked into the infant's circulation during labor as a result of increased intrauterine pressure, there is no evidence that cesarean section will prevent this. In fact, cesarean section opens the uterine blood sinuses and in this way may permit maternal blood to gain access to the fetal blood stream.

Dr. Levine pointed out that kernicterus can also occur when the maternal serum contains blocking antibodies only and asked how this may be explained. Such cases are exceptional, but we can now explain them. What happens in these cases is that the baby is born with its red cells coated with univalent antibodies. Fetal serum contains little or no conglutinin, but as soon as the baby is born the conglutinin begins to form. If the baby becomes extremely dehydrated and has a fever, the plasma proteins become more concentrated and aggregate to form conglutinin, and this conglutinin (colloidal aggregate of plasma proteins) is adsorbed by the sensitized red cells and causes the red cells to stick together. The resulting intravascular conglutination produces the same effects as intravascular agglutination. It may be, therefore, that in some cases kernicterus in the newborn can be prevented if the infant is not allowed to become dehydrated.

There is no way in which one can treat the fetus in utero, and we were misunderstood as to the use of exchange transfusion. That is to be performed on the infant as soon as it is born. To perform a satisfactory exchange transfusion, one must transfuse and simultaneously withdraw two or three times as much blood as the baby's entire body contains because after a while one is taking out some of the blood one is injecting. Of course, one cannot take out all the infant's blood at one time.

As for the cases of athetosis and dystonia in which there is no history of neonatal jaundice, Dr. Bakwin and I have found the normal percentage of Rh-negative mothers and none of these were sensitized to the Rh factor. Thus, in these cases the disturbance is not due to isosensitization; the clinical histories suggest, instead, that birth injury may be the pathogenic agent.

I have not time enough to cover the rest of the points, for which I am glad, because some of the questions were too difficult.

DR. MATTHEW BRODY: One of the tough problems we have to explain is the absence of kernicterus in infants with congenital atresia of the bile duct, in whom the jaundice is intense. It is true that there is little reactive change to the lesions we demonstrated tonight. However, we have seen these lesions in 4 fatal cases in which the child's mother showed large amounts of agglutinins. In various cases

these lesions can be demonstrated in every organ of the body: the brain, the lungs, the intestine and the kidneys. We feel that this structural change must be correlated with the serologic findings.

Dr. Globus pointed out that he was unable to demonstrate neurologic signs or cerebral lesions in the 6 cases he studied. I do not know whether or not the infants died of neurologic disease, but the mere fact that they had kernicterus and died is evidence that they died of something.

These vascular obstructions are not ordinary clots; they are agglutination thrombi, and they differ from ordinary clots, in which various mechanisms are involved.

The white matter is involved, but perhaps not so much as the gray matter.

Correlation of Clinical and Electroencephalographic Findings in a Large Series of Cases of Verified Cerebral Tumors. DR. PAUL F. A. HOEFER, DR. EDWARD B. SCHLESINGER (by invitation), DR. HARRY PENNES (by invitation) and MISS MARY D. COX (by invitation).

This paper was presented as a preliminary report on this investigation, a detailed presentation of which will appear in a future issue of the ARCHIVES.

DISCUSSION

DR. HANS STRAUSS: I cannot easily discuss this paper because I did not see it before its presentation and because the figures were projected so rapidly on the screen. I could record only one of these figures, namely, 67.5 per cent, which represented the authors' correct localization of hemispheric tumors. This compares with 68.3 per cent in similar material studied in the electroencephalographic laboratory of Dr. Wechsler's service at the Mount Sinai Hospital. It is gratifying to see that these figures are almost identical, though the methods in taking and evaluating the records vary. As a rule, my associates and I use eleven electrodes and rely for localization on measurements of the delta index (Strauss, H.: Electroencephalographic Studies: A Method for Differential Diagnosis of Abnormal Electroencephalograms, *J. Mt. Sinai Hosp.* **9**:17-22, 1942) rather than on triangulation. In view of our almost identical results, I wonder whether for practical diagnostic purposes the authors needed to use so many electrodes.

Our surveys show at present 253 verified intracranial tumors, 164 of which are tumors of the cerebral hemispheres; the latter include 47 meningiomas and 117 gliogenous and metastatic tumors. In contradistinction to Dr. Hoefer's survey, we include among our tumors only true neoplasms, and not such lesions as subdural hematoma and cerebral abscess. Normal records were obtained in 63 cases, which represent approximately 25 per cent of all the intracranial tumors. However, the percentage of normal records varied greatly with the type and localization of the tumor. Normal records were obtained with about 80 per cent of the cerebellopontile angle tumors and with only 12 per cent of the hemispheric tumors. Among the latter, there was a significant difference between meningiomatous tumors, with 23.5 per cent of which normal records were obtained, and gliogenous and metastatic tumors, with approximately 7 per cent of which the records were normal. A correct localization was made in 62 per cent of the meningiomatous and in 72 per cent of the other tumors. The difference in the number of normal records and correct localizations in the two series can be explained by the larger degree of electroencephalographic abnormality associated with tumors of faster growth. The gliogenous and metastatic tumors as a rule interfere more seriously with the metabolic function of cerebral tissue and so create a much higher degree of abnormality in the electroencephalogram.

In a previous paper (*J. Mt. Sinai Hosp.* **9**:17-22, 1942) I classified the electroencephalograms according to the degree of abnormality on the basis of certain standard measurements. According to such standards, the degree of abnormality was high in 30 per cent of the meningiomatous tumors and in 71 per cent of the gliogenous and metastatic tumors. In a paper published with Dr. Greenstein (Greenstein, L., and Strauss, H.: Correlations Between the Electroencephalogram

and the Histological Structure of Gliogenous and Metastatic Brain Tumors, *J. Mt. Sinai Hosp.* **12**:874-877, 1945), we demonstrated a correlation between the histologic structure of metastatic and gliogenous tumors of the hemisphere, as studied in the neuropathologic laboratory of Dr. J. H. Globus, with the degree of abnormality of the encephalogram, as measured by the focal delta index. I wonder whether Dr. Hoefer has made similar observations.

Only if the electroencephalographic changes are correlated with the clinical findings are they of the greatest diagnostic value. Is it also Dr. Hoefer's experience that meningioma with jacksonian seizures is associated with normal records in a much higher percentage of cases than is meningioma without such seizures?

DR. LEO M. DAVIDOFF: Dr. Margaret Rheinberger and I began to use electroencephalography in the localization of cerebral tumors in 1938, and our total figures are about the same as the number of cases that Dr. Hoefer has presented. We have a little over 350 cases in which we have histologic verification of the lesion only. I shall not attempt to discuss the technical side of this problem. If Dr. Rheinberger wishes, she may do so. Aside from any interesting physiologic facts that may have been observed as a result of these studies, I should like to ask Dr. Hoefer what have been the practical, clinical results in the application of this method of investigation in the treatment of cerebral tumors. I can only cite from our experience as follows, and this may be significant. As I said, we started to use this method in 1938. During the first two years we worked with a triple pen writing apparatus, and we were feeling our way; so the first two years of our studies were perhaps less productive than the later years. Thus, in comparing our brain tumor material prior to 1940 with that after 1940, we have made the following observation: Before 1940, which means usually that we were without the help of electroencephalography, we felt it necessary to make air studies in 56 per cent of our cases of cerebral tumor before operation. Since 1940, and that takes us up to about nine or ten months ago, when we moved our laboratory to Montefiore Hospital, we have found it necessary to use air injections in only 21, as against 56, per cent, indicating that we have reduced our preoperative pneumoencephalographic studies by a very considerable percentage. From that point of view, we feel that, whatever physiologic facts we may learn from this method of investigation, we have at least one practical result, that is, that we can spare a very considerable number of our patients the discomfort, and even the danger, of pneumoencephalography.

DR. MARGARET RHEINBERGER: I cannot add much to what has been said. Both Dr. Hoefer's and Dr. Strauss's figures are much like ours. There is one question I should like to ask Dr. Hoefer: What is a false localizing sign? I do not think there is such a thing. No sign can be false if it is correctly interpreted. Only when one considers all indications of abnormality in any pattern (whether or not they appear where one would expect in correlation with a more obvious disturbance) and endeavors to evaluate each in relation to the others and to the pattern as a whole does one have, in my opinion, the background on which to base judgment as to the probable location, or possible locations, of a discrete lesion which could produce all the abnormalities observed. Our results do not contain any false localizations; otherwise, as I said, they are much like those of other workers.

DR. PAUL F. A. HOEFER: To answer Dr. Strauss's questions first: We had planned to present a number of clinical correlations but had to put it off because of the shortness of time and because we had not reviewed our entire clinical material. I do not fully agree with Dr. Strauss as to the significance of jacksonian seizures in cases of meningioma. We have seen a good number of cases; one was presented tonight. However, I was struck by the fact that the incidence of seizures was lower with the meningiomas and higher with the astrocytomas than we had expected.

In reply to Dr. Davidoff's question: The material presented tonight was seen between 1940 and 1943. In these years about two thirds of our patients had air studies. I do not know how figures compare for the more recent material.

Dr. Rheinberger asks, "What is a false localizing sign?" I believe the best definition I can give is this: It is focal activity conducted from its site of origin by long tracts or commissures to an area far removed from where the lesion actually is. It would mislead one if one were to look for the tumor in the area where the signs appear. If, as in the case of a cerebellar tumor or a tumor of the eighth nerve, the site of the original lesion is inaccessible to electroencephalographic study, the "false" signs may be the only localizing signs. In other instances, as in those of lesions of the temporal lobe, one can distinguish between the true focus and its "mirror" image on the opposite side. In a study conducted with Pool (Hoefer, P. F. A., and Pool, J. L.: Conduction of Cortical Impulses and Motor Management of Convulsive Seizures, ARCH. NEUROL. & PSYCHIAT. **50**:381-400 [Oct.] 1943), I was able to show a number of conduction mechanisms for cortical electrical activity, and this is the probable explanation for false localizations of cerebral tumors.

Book Reviews

Psychiatric Interviews with Children. Edited by Helen Leland Witmer. Price $4.50. Pp. 443. New York: Commonwealth Fund, 1946.

Direct psychotherapy with children is a new field in psychiatry, enveloped in an abundance of theory, little standardized in its application, and therefore difficult for the student to grasp. This recent publication of the Commonwealth Fund, elucidating psychotherapeutic processes through detailed case records, will provide the worker in the field with real help in his effort to translate theoretic considerations into practice.

The editor, Helen Leland Witmer, has collected 10 case records from the files of eight experienced therapeutists, Frederick H. Allen, Phyllis Blanchard, Lydia M. G. Dawes, Hyman S. Lippman, Martha W. MacDonald, H. B. Moyle, Beata Rank and Robert A. Young. Each record describes in detail the progress of the therapeutic relationship, from the initial interview to the termination of treatment, with a brief follow-up study appended. Accompanying each record are footnotes by the therapeutist discussing the procedures followed and interpreting productions and behavior. In addition, there are intake and progress reports by the social worker who guides the mother throughout the period of the child's treatment. This direction for the parent is closely integrated with the psychiatrist's work with the child, and its importance in the total therapeutic process stands out clearly.

The 10 cases, classified under the headings "non-neurotic," "with neurotic symptoms" and "seriously neurotic," are fairly representative of child guidance clinic practice, although in two respects they are selected: In all cases either the home was intact or one parent at least was actively interested in the child, and in all cases treatment was successful. Common clinical problems are analyzed, including reading disability, feelings of inadequacy, sex identification, sibling rivalry, handling parental authority, the process of differentiation from parents and the severer anxiety states.

The editor prefaces the studies with an introduction to the subject of child guidance and "the dynamic of therapy." She provides in this section an excellent brief survey of the field, adding substantially to the importance of the volume.

The approach throughout the book is dynamic with various emphases, depending on the point of view of the individual therapeutist. In few cases is a rigid scheme set up, and generally the therapeutic relationship is used to provide a means of release for the child through play rather than through probing or explanation. Also, through joint action with the social worker the reality situation is at all times stressed.

The importance of these principles of technic as determinants of success of treatment emerges clearly in the case studies, but one other factor stands out in perhaps even stronger relief—the art of the therapeutist. Here, as in a few other writings, the personal quality of the therapeutic relationship is brought into sharp focus for the reader's analysis and study. It is this frank exposition of the art of psychotherapy that makes "Psychiatric Interviews with Children" an unusual and outstanding addition to the literature of child psychiatry and psychotherapy in general.

Mongolism and Cretinism: A Study of the Clinical Manifestations and the General Pathology of Pituitary and Thyroid Deficiency. By Clemens E. Benda, M.D. Price, $6.50. Pp. xv, plus 310, with 101 illustrations. New York: Grune & Stratton, Inc., 1946.

Cretinism has been one of the mysteries of abnormal development. Appearing in all races and in the "best" of families, it has puzzled physician and geneticist alike. Benda does the medical profession a great service in lifting the veil of this

mystery and in analyzing the disorder on the basis of some 300 cases personally observed at the Wrentham State School. Since mongolism and cretinism are often confused, he includes parallel studies on these two related disorders of the endocrine system, with clarification of the details of each. He reaches the conclusion that mongolism is due to hypofunction of the pituitary body and cretinism to hypofunction of the thyroid gland, and that the physical characteristics of mongolism, better termed acromicria, are the reverse of acromegaly. In order to accomplish this demonstration, he surveys the field with great thoroughness, basing his discussion on necropsies in 48 cases. The lesions in the pituitary body are striking, and are characterized as follows: "1. Deficiency of the gamma cell system and general inability of formation of chromophilic elements. 2. Chromophilic shift toward eosinophily with absence or deficiency of gamma cells and pathology of beta cells. . . . Mongolism is the congenital type of hypopituitarism."

It has long been recognized that the pituitary gland is the "master gland" of the body, and that its various hormones stimulate the thyroid, adrenal glands, gonads and mammary glands, as well as performing other functions. When the pituitary gland is congenitally deficient, the child is unfinished, and this is apparent in most of the tissues of the body, including the brain. Benda includes also morphologic and chemical studies on the blood. The results of these are shown in numerous graphs and tables, but the observations are not outstanding and would not be of value in doubtful cases because of the overlapping of figures for the two diseases, mongolism and cretinism.

Mongolism, Benda shows conclusively, is determined by a disturbance in the maternal condition. Age; multiple births; ill health, particularly psychosomatic disorders; abortion; bleeding; threatened abortion, and prematurity appear with such frequency in the case histories as to indicate that when a mongolian idiot is born the mother is close to sterility. It is not yet possible to forecast the birth of a child with mongolism on the basis of any single factor, but when two or more are present the physician may be warranted in preparing the pregnant woman for bad news. The mongolian idiot is a "salvaged abortion," and not too much should be done to prevent a threatened abortion if several unfavorable factors are present in the maternal condition. As far as treatment is concerned, the mongolian idiot cannot be expected to achieve physical or mental maturity until some effective pituitary preparation is discovered. Thyrotropic hormone is promising, but most reliance is placed on thyroid substance because of its easy control. Poor heat regulation may contribute to the many infections that occur in mongolian idiots, so that attention to extra warmth and exercise and frequent feedings high in carbohydrate and salts and low in fats may be desirable.

Benda's monograph is detailed, specific and accompanied with many illustrations. The literature on mongolism is cited abundantly, with significant contributions on cretinism included. It is an outstanding contribution to the clarification of a disorder afflicting an estimated 60,000 inhabitants of the United States.

Textbook of Abnormal Psychology. By Carney Landis and M. Marjorie Bolles. Price, $4.50. Pp. xi, plus 576. New York: The Macmillan Company, 1946.

The plan for presentation of the field of abnormal psychology in this volume differs from that in less recent textbooks in extending the range of content and in covering similar content from a multiple approach. Thus, one section is devoted to terms and concepts to be utilized in description and classification; another section is concerned with various diagnostic categories; still another, with various aspects of psychopathology without direct reference to their diagnostic category; several chapters elaborate general basic explanatory concepts, and, finally, contributions from the various sciences, from education and from the law are evaluated. The addition of chapters on medical psychology, the law and mental abnormality, and the role of the brain in psychopathology is particularly welcome. These

chapters summarize new material that is pertinent to the area of abnormal psychology.

Each chapter is systematically organized to cover the factual data; the history, and the physiologic, the analytic, the neurologic, the biologic and the psychologic experimentation and contribution, with the novel addition of a subjective description of a personal experience by a victim of the disorder whenever feasible. In addition to this meticulously systematic approach, the glossary, comprehensive index, chapter summaries and bibliographies make for ease of use by the student.

Proper emphasis is placed on the extent of unsolved problems in the abnormal field. However, the sheer quantity of painstaking summaries of experimental studies in the biologic, physiologic and neurologic fields, which have admittedly thrown all too little light on the basic problems, tends to water down the impression of positive values contributed by some of the more dynamic approaches.

This volume is recommended for use by students for its comprehensiveness and inclusion of valuable new material.

Chronic Disease and Psychological Invalidism: A Psychosomatic Study. By Jurgen Ruesch, M.D., and collaborators. Published with the sponsorship of the American Society for Research in Psychosomatic Problems. Pp. 191. New York, 1946.

This monograph is the result of a study made at the Langley Porter Clinic by members of the Division of Psychiatry of the University of California Medical School, under a grant from the Office of Scientific Research and Development.

One hundred and eighty-seven patients were studied after referral from other hospital departments because of chronic disease, the physical symptoms of which had persisted for an undue length of time. All patients with psychoneuroses and psychoses without physical symptoms and with psychoneuroses which had never been treated for physical symptoms were excluded. One hundred and twenty-three of the patients were seen for a short period, and a complete medical work-up, psychiatric diagnosis, psychologic tests and evaluation of social class membership and cultural factors were made. The other 64 patients were studied intensively and subjected to individual and group psychotherapy, and information concerning their character structure was given special attention.

The results of these studies are reported in this monograph, both in statistical form and with regard to the dynamic factors involved. There is also a discussion of certain of the specific problems most frequently encountered, such as those of the frigid woman, venereal disease, abused operations, abuse of medicine, diets and rest, and the perpetually referred patient. An attempt is also made to determine the prognostic possibilities for treatment in 53 of the patients, especially with psychologic tests, and to relate these to the actual therapeutic results obtained, with a description of the therapeutic methods used. Finally, there is a stimulating discussion of the psychodynamic factors presented by these patients and the reciprocal relationships with the actual physical disease present, and a provocative attempt is made to correlate delayed recovery with social class membership and attitudes

This monograph is a valuable addition to psychosomatic literature and can be read with profit by all physicians.

A Textbook of Psychiatric Nursing. Formerly entitled "A Textbook of Psychiatry." Fourth edition. By A. P. Noyes, M.D., and E. M. Hayden, A.B., R.N. Price, $3. Pp. 396. New York: The Macmillan Company, 1946.

The authors, a psychiatrist and a psychiatric nurse, have changed the title of their latest edition because of an increased emphasis on nursing procedures in this, the fourth, edition. This title is apt to be misleading, since, except for the added chapter on nursing procedures, the emphasis is still chiefly on psychiatry. In the fourth edition the chapter on the development of the mind has been omitted, without destroying the value of the text. Discussion of the organic psychoses is now

confined to two chapters less than formerly but gives adequate consideration to the more common conditions.

Throughout the volume there is commendable emphasis on the thinking, feeling and behaving of human beings, rather than strictly on the investigation, diagnosis and treatment of psychiatric patients. The instructions to the nurse along the lines of the patient's thinking, feeling and behaving are too general. The chapter entitled "Principles of Psychiatric Nursing" is also too general, owing perhaps to the fact that so many subjects are included in a single chapter.

The basic principles of care incorporated in psychiatric procedures do not vary greatly. It is not very clearly brought out in this book, however, that changes in application, safety measures and equipment associated with these procedures will be found according to the location and physician. Nursing functions prior to and following the treatments discussed would make this book more valuable to students of nursing.

The organization and arrangement of the text follow lines of previous editions, which have proved satisfactory to a great degree. Affiliating nursing students have found this text very helpful, and the new edition should prove increasingly so.

There are a serviceable glossary and index. Some of the explanations of psychiatric terms fall short of clarity; e. g., "hysteria: a form of psychoneurosis producing various symptoms, many of which simulate physical disease" (page 379) and "extravert: one whose personality is characterized by extraversion" (page 378).

News and Comment

INTERNATIONAL CONFERENCE ON PSYCHOSURGERY

An international conference on psychosurgery will be held in Lisbon, Portugal, in April 1948, at the invitation of the Portugese government and the University of Lisbon. Secretary of the United States Committee is Dr. Walter Freeman, 2014 R Street, N. W., Washington, D. C.